‘LIPID PROFILE IN PREGNANCY’

DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQIUREMENTS OF TAMIL NADU DR.M.G.R MEDICAL UNIVERSITY FOR THE DEGREE OF M.S. BRANCH II (OBSTETRICS AND GYNAECOLOGY) EXAMINATION TO BE HELD IN APRIL 2014

CERTIFICATE

This is to certify that the dissertation entitled "LIPID PROFILE IN PREGNANCY" is the original work of Dr.Catherine.S done under my guidance towards the M.S. Branch II (Obstetrics and Gynecology) Degree Examination of Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in April 2014.

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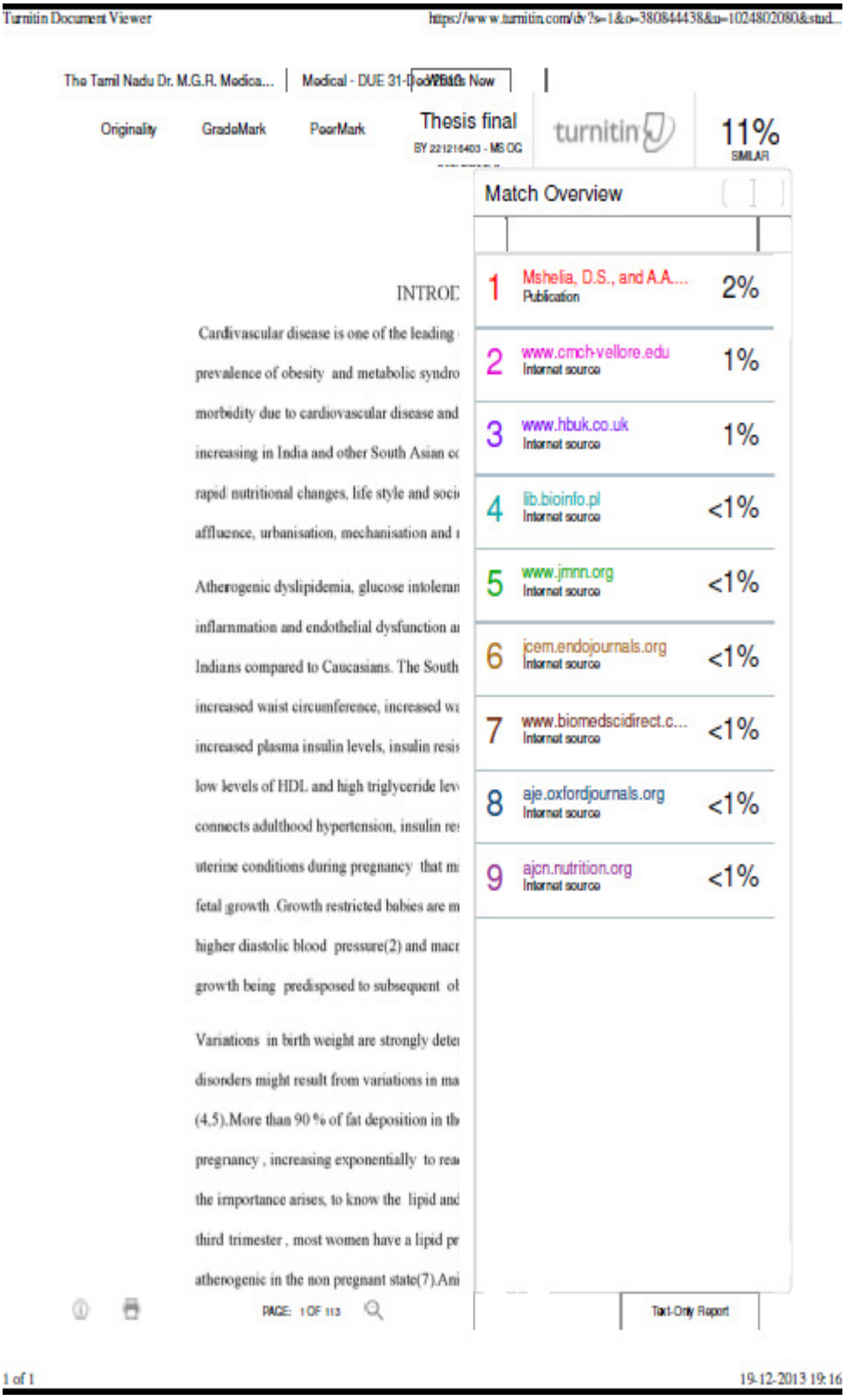

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Lipid profile in pregnancy and its effect on infant birth weight
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Dear Dr. Catherine. S,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Lipid profile in pregnancy and Its effect on infant birth weight" on October 1, 2012.

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3. Information Sheet and Consent Form (English and Tamil)
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1 of 1

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Dr. Paul Ravindran	PhD, Dip RP, FCCPM	Professor, Radiotherapy, CMC	
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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent. And on completion of the study you are expected to submit a copy of the final report.

A sum of Rs 33,333/- (Rupees Thirty Three Thousand Three Hundred and Three only) will be sanctioned for 10 Months

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

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ACKNOWLEDGEMENTS

First and foremost, I thank my Lord Jesus Christ , for showering me with His abundant grace and thus enabling me to complete this thesis.

I owe gratitude to Dr. Annie Regi (Guide) and Dr. Elsy Thomas (Co- guide) for all their guidance and support.

I extend my heartfelt and sincere thanks to Dr. Thomas Paul for idea conceptualisation and Dr. Nihal Thomas, for their assistance in funding, formatting , and editing this work.

This would not have been feasible if not for the help rendered by Dr. Selvakumar and his team ,from the Department of Biochemistry in the area of sample analysis.

The assistance provided by the biostatisticians Dr. Antonisamy, Dr. Tunney and Miss Gowri was invaluable. This is also an opportunity for me to place on record the aid of the Medical Record Officers Mr. Kusmos and Mr. Christopher and the radiology assistants Mrs. Narayani, Mrs. Lilly and Mrs. Maya in the recruitment and follow up of the involved women.

Miss Banu and Mr. Muthukumar played a key role in data entry and data analysis. In addition, I would like to acknowledge the efforts put in by my co-PG registrars in the follow up of the women involved in the study. I also acknowledge the assistance by Mrs.Usha , our office secretary , an ever smiling and ever helpful person.

Last but not the least my family, my husband Dr. Arun Immanuel ,my two daughters Bettina and Danita, my parents and my in-laws , for all their prayers, patience and love.

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INTRODUCTION

Cardivascular disease is one of the leading cause of death among women.The prevalence of obesity and metabolic syndrome leading to increased mortality and morbidity due to cardiovascular disease and type 2 Diabetes Mellitus is very rapidly increasing in India and other South Asian countries. This is predominantly due to rapid nutritional changes, life style and socio economic transition ,increasing affluence, urbanisation, mechanisation and rural to urban migration.

Atherogenic dyslipidemia, glucose intolerance, thrombotic tendency ,subclinical inflammation and endothelial dysfunction are proportionately higher amongst Asian Indians compared to Caucasians. The South Asian phenotype is characterised by increased waist circumference, increased waist to hip ratio, excessive body fat mass, increased plasma insulin levels, insulin resistance and atherogenic dyslipidemia with low levels of HDL and high triglyceride levels.(1) The 'Fetal origins' hypothesis connects adulthood hypertension, insulin resisitance, dyslipidemia to adverse intra uterine conditions during pregnancy that might be associated with disproportionate fetal growth .Growth restricted babies are more prone for adult metabolic disorders, higher diastolic blood pressure(2) and macrosomic babies with accelerated fetal growth being predisposed to subsequent obesity and gestational Diabetes mellitus.(3)

Variations in birth weight are strongly determined by neonatal fat mass . Fetal growth disorders might result from variations in maternal and fetal lipid metabolism (4,5).More than 90 % of fat deposition in the fetus occurs during the last 10 weeks of pregnancy , increasing exponentially to reach a rate of 7 g/day close to term(6).Hence the importance arises, to know the lipid and lipoprotein ratios in pregnancy. By the third trimester , most women have a lipid profile which is considered highly atherogenic in the non pregnant state(7).Animal model studies show that maternal

hypercholesterolemia during pregnancy , though temporary triggers pathogenic events in the fetal aorta enhancing atherogenesis later in life.(8)

As early as 1934,Eldon.M.Boyd published an article on "The Lipemia of pregnancy" as maternal serum was described as milky "adipositas sanguinas". He concluded that 'neutral fat' begins to rise in pregnancy and reaches 100%(compared to non pregnant women) by the third trimester, whereas phospholipid and cholesterol increase from the 2nd trimester onwards and may reach a level , which is 25% greater than non pregnant women by 3rd trimester.(9)

A supraphysiological rise in plasma lipids (>95th percentile) in pregnancy may serve as a marker for "pre lipemia" in the same way gestational diabetes is a marker for pre diabetes(10).

Physiological increases in maternal TC,HDL,LDL&TGL are needed for development of cell membranes, steroid synthesis, cell proliferation& differentiation, metabolic regulation & fetal growth(11). The increase in lipid and lipoprotein ratios in pregnancy is highly influenced by (a) Genetic factors .(b)Medical complications of pregnancy.(c) Pre existing medical conditions. Overweight and obese women have different lipid profiles during pregnancy than their normal-weight peers. This difference may be the result of metabolic dysregulation associated with maternal overweight and obesity that mediates the increased risk of adverse outcomes found in these women.(12)

Hence this study "**LIPID PROFILE IN PREGNANCY** " was carried out, to obtain the range of lipid profile values (in three trimesters) in normal pregnancy in South Indian pregnant women .With the rise in the incidence of GDM among Asian women

,this study will also help in determining the early changes in lipid profile that might predict developing GDM later on in pregnancy.

In view of the strong evidence correlating infant birthweight with adult onset hypertension, dyslipidemia, insulin resistance and obesity ,this study aims at finding if there is an association between maternal lipids to changes in infant birth weight.

AIMS AND OBJECTIVES

i)To assess the longitudinal changes in lipid profile during the three trimesters of normal pregnancy.

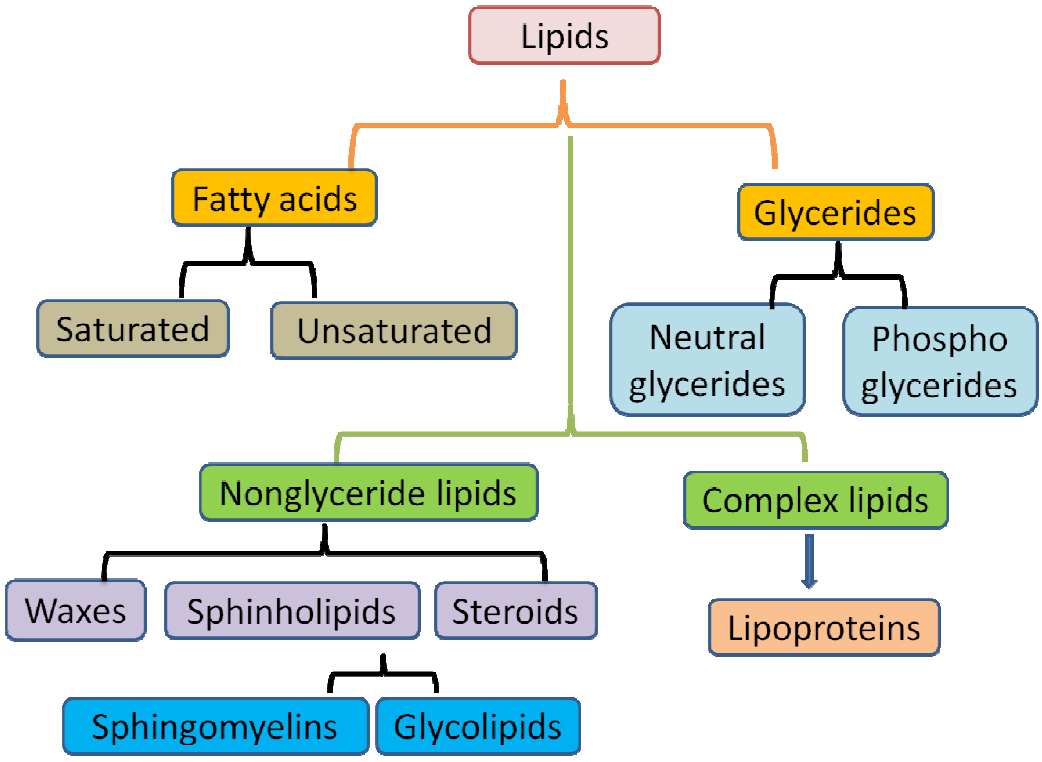
ii)To determine , if alterations in lipid profile in each trimester may be associated with changes in new born's birthweight.

iii)To determine if adverse pregnancy outcomes such as gestational hypertension and gestational diabetes mellitus, are associated with altered lipid profile.

LITERATURE REVIEW

Definition of **LIPID**: " any of various substances that are soluble in non polar organic solvents (such as chloroform and ether), that are usually insoluble in water, that with proteins and carbohydrates constitute the principal structural components of living cells, and that include fats, waxes, phosphatides, cerebrosides, and related and derived compounds"(13).The term 'LIPID' was first used by German Biochemist Bloor in 1943.

Lipids are classified into 8 broad categories;

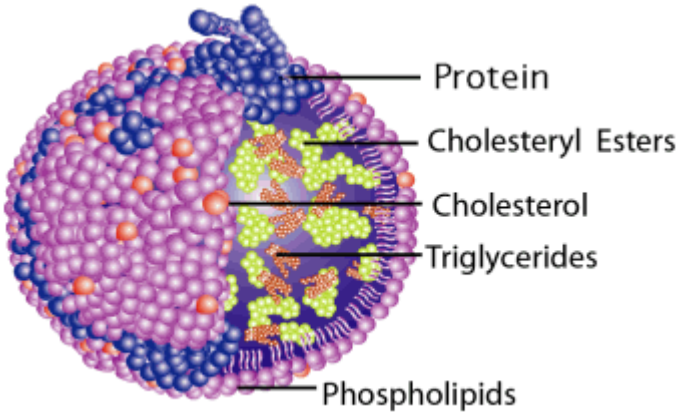


Source :Biologyexams 4 u,Google images

Fatty acyls FA ,Glycerolipids, Glycerophospholipids ,Sphingolipids,Sterol lipids ,Prenol lipids ,Saccharolipids ,Polyketides (14).

Lipids, such as cholesterol and triglycerides, are insoluble in plasma .They are carried by lipoproteins to various tissues for energy utilization, lipid deposition, steroid hormone production, and bile acid formation.

Structure of a lipoprotein:



Source : Antonio Zamora,Scientificpsychic.com

Lipoproteins have a lipid and a protein component. The lipid component is occupied by cholesterol, Triglycerides and phospholipids. The protein component is called Apolipoprotein. These apoproteins act as cofactors for enzymes and ligands for receptors.

Lipoproteins are classified into 5 groups:

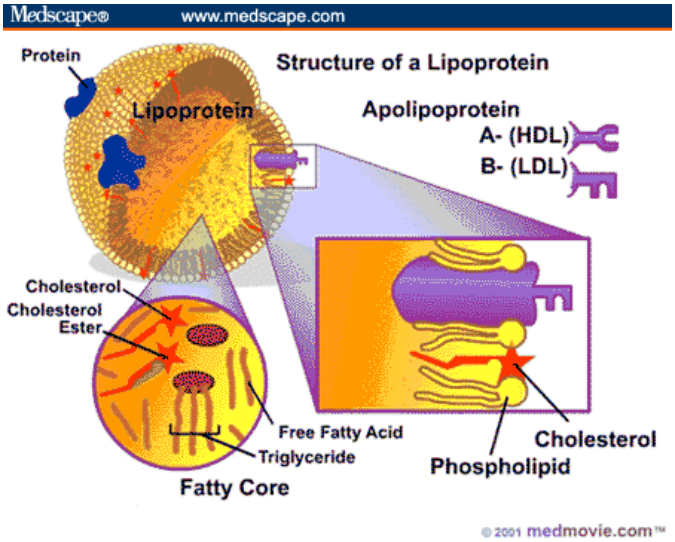
1. Chylomicrons.

2. VLDL.

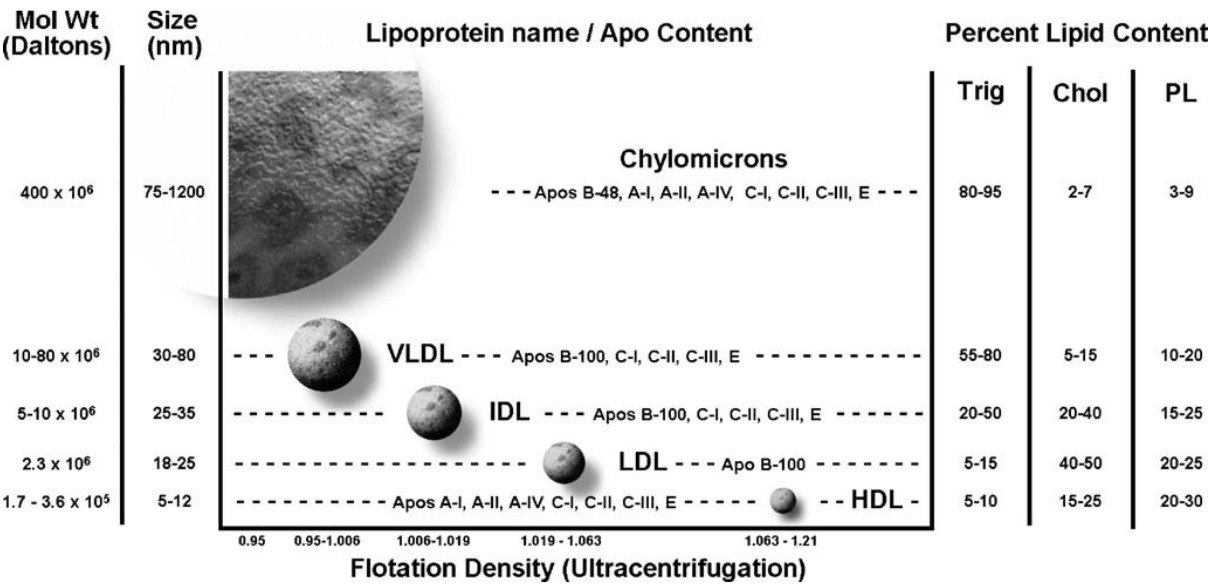
3. IDL.

4. LDL.

5. HDL.



Source :Medscape.com

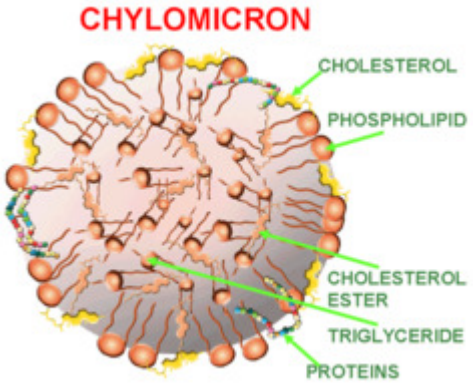


Source : JM Saland, H. G. (2007). "Lipoprotein metabolism in chronic renal insufficiency." Pediatr Nephrol 22: 1095-1112

Lipoprotein class	Density (g/mL)	Diameter (nm)	Protein % of dry wt	Phospholipid %	Triacylglycerol % of dry wt
HDL	1.063-1.21	5 – 15	33	29	8
LDL	1.019 – 1.063	18 – 28	25	21	4
IDL	1.006-1.019	25 - 50	18	22	31
VLDL	0.95 – 1.006	30 - 80	10	18	50
chylomicrons	< 0.95	100 - 500	1 - 2	7	84

Source :TooSogiE Lipid diagnostics

1.Chylomicrons : They are large particles and they carry dietary lipid from intestine to liver, skeletal muscle and adipose tissue.

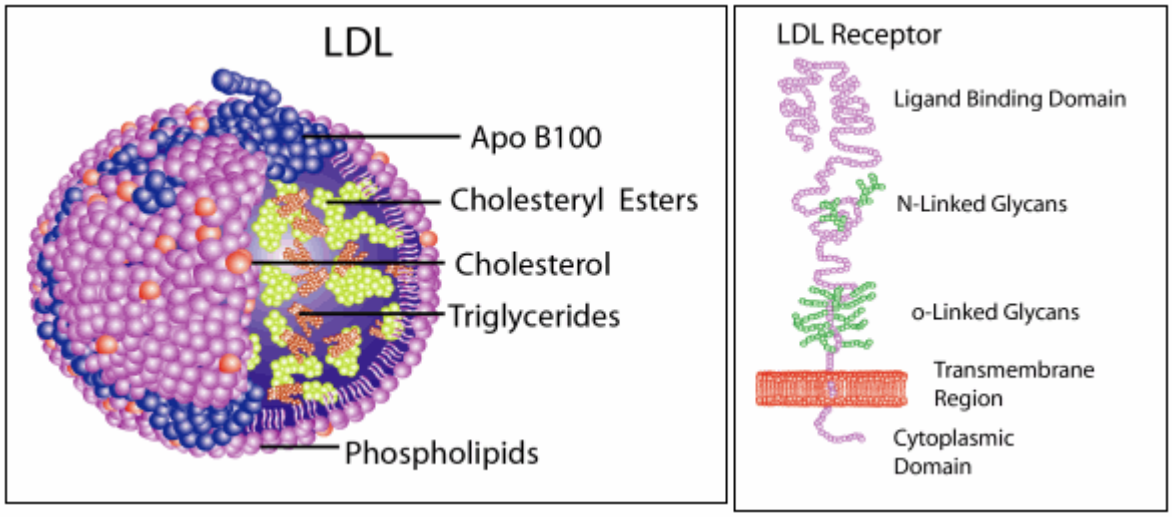


Source : people upei.ca

2.VLDL (Very Low Density Lipoprotein):They carry most of the endogenous , newly synthesised triglycerides and cholesterol to a lesser extent from liver to adipose tissue.

3.IDL (Intermediate Density Lipoprotein):They carry cholesterol esters and triglycerides.

4.LDL(Low Density Lipoprotein): They carry cholesterol esters from liver to cells of the body.



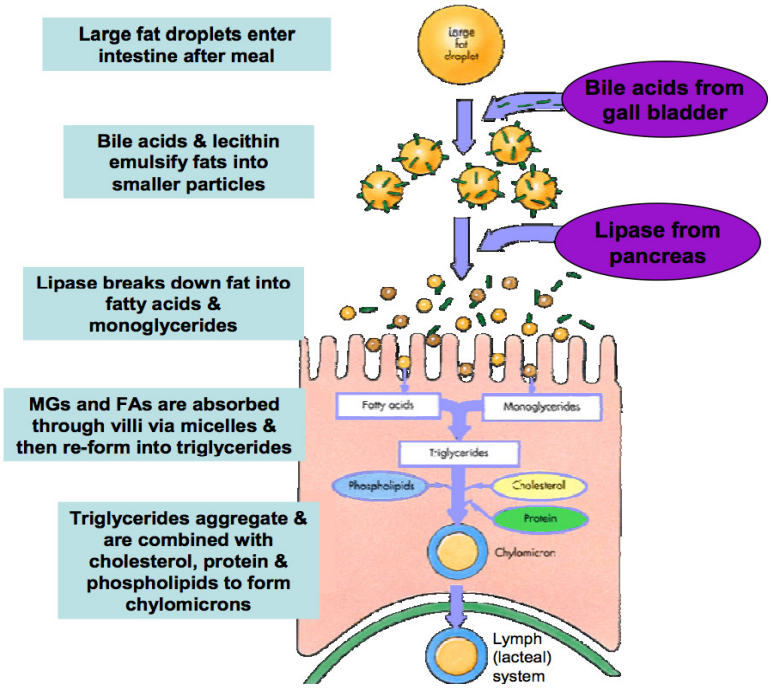
Source :Sigma aldrich.com

5.HDL (High Density Lipoprotein): They carry cholesterol esters from the peripheral tissues and return to the liver.

LIPID METABOLISM:1.Exogenous pathway.

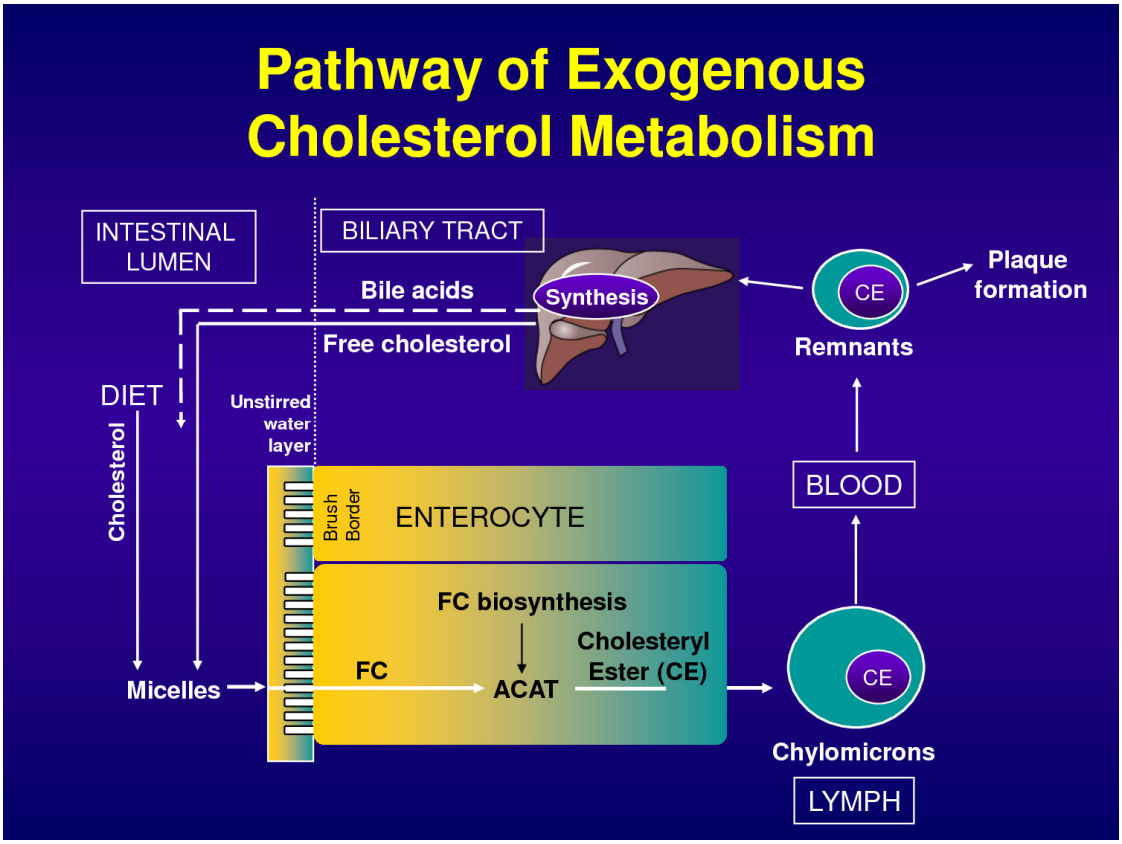
2.Endogenous pathway .

EXOGENOUS PATHWAY:



Source : syontix.com

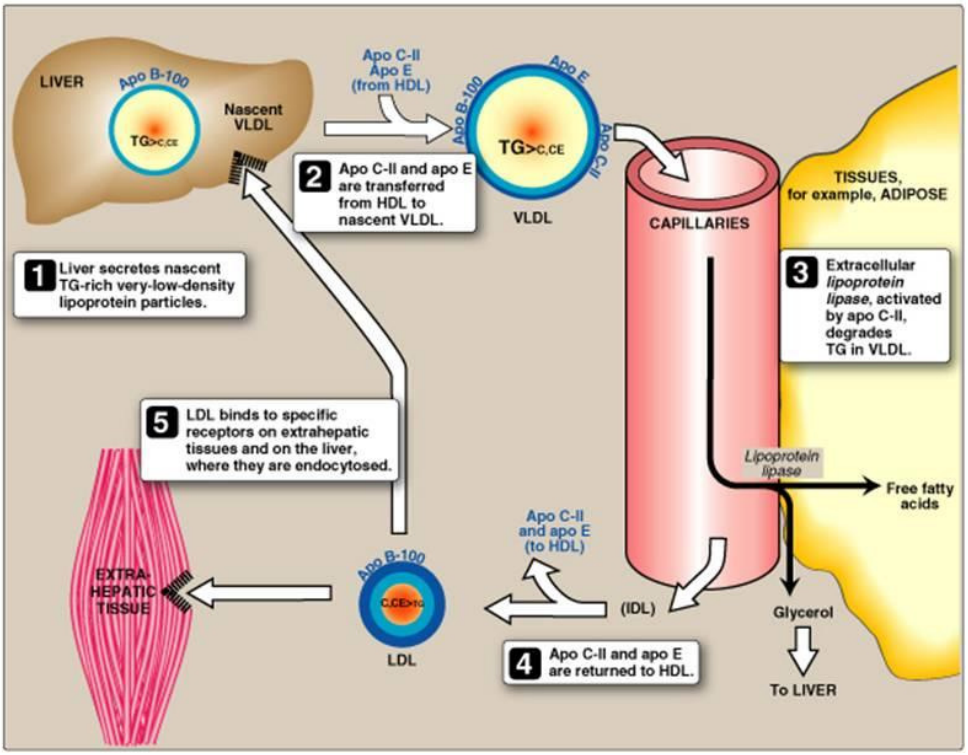
The pathway starts with intestinal cell absorbing dietary cholesterol and free fatty acids. Within the cell, fatty acids combine with glycerols to form triglycerides. Cholesterol undergoes esterification by the action of Acyl co A cholesterol acyl transferase(ACAT) to form cholesterol esters. Triglycerides and cholesterol esters are assembled into chylomicrons within the cell. The main apoprotein attached to the chylomicron being B-48 which prevents the chylomicron getting attached to LDL receptors.



Source : www.docstoc.com

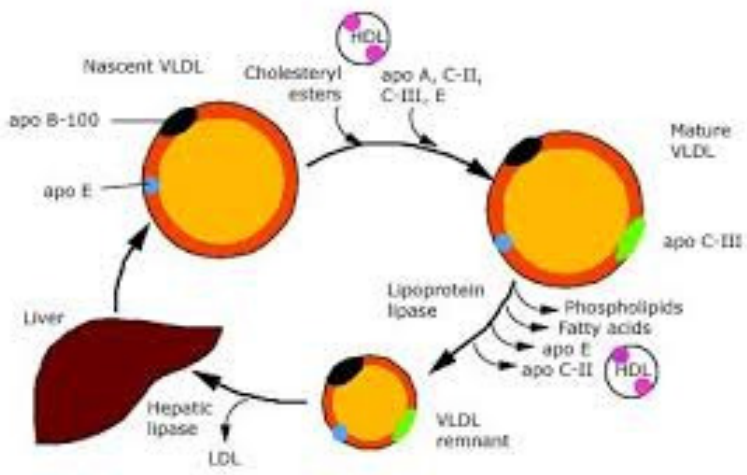
Once the chylomicrons enter the circulation, apo C-II and Apo –E are acquired. Apo C-II acts as a cofactor for Lipoprotein lipase from the tissues to act on the chylomicrons which then releases the free fatty acids produced by the hydrolysis to breakdown the core triglyceride. Free fatty acids are absorbed by the tissues as energy source or converts back to triglycerides for storage. The end product of chylomicron breakdown, the smaller chylomicron remnants are absorbed by their respective receptors in the liver which is later used in the production of HDL.

ENDOGENOUS PATHWAY:



Source : www.studyblue.com

This begins with the hepatic production of VLDL.VLDL contains 60 % of triglycerides and 20 % of cholesterol esters. Microsomal triglyceride transfer protein (MTP) (15)is an intracellular lipid transfer protein that aids in transfer of triglycerides mainly to apolipoprotein B found in the liver.



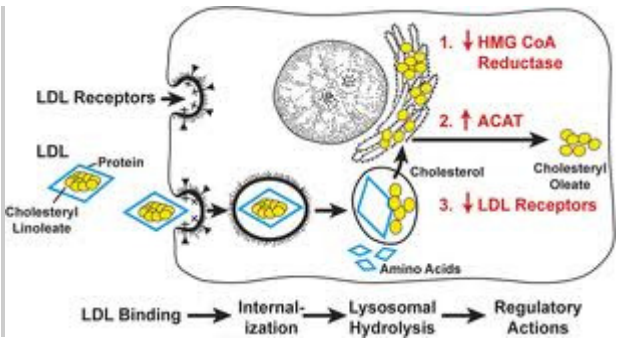
Source : www.fracp.bigpondhosting.com

The other surface apolipoprotein C-II acts as a cofactor for the action of Lipoprotein lipase, Apo C-III inhibits it, Apo B and E serve as ligands for LDL receptors. VLDL is acted upon by lipoprotein lipase in tissues such as adipose tissue and muscle where the lipid core , mainly triglycerides are broken into glycerols and fatty acids. When VLDL loses most of it's triglyceride, it becomes smaller to become IDL, which is then absorbed by the liver to form LDL with more cholesterol content using hepatic lipase.LDL enters the circulation to be taken up the tissues via the LDL receptors. Any excess LDL is reabsorbed in the liver.

LDL (Low density lipoprotein):

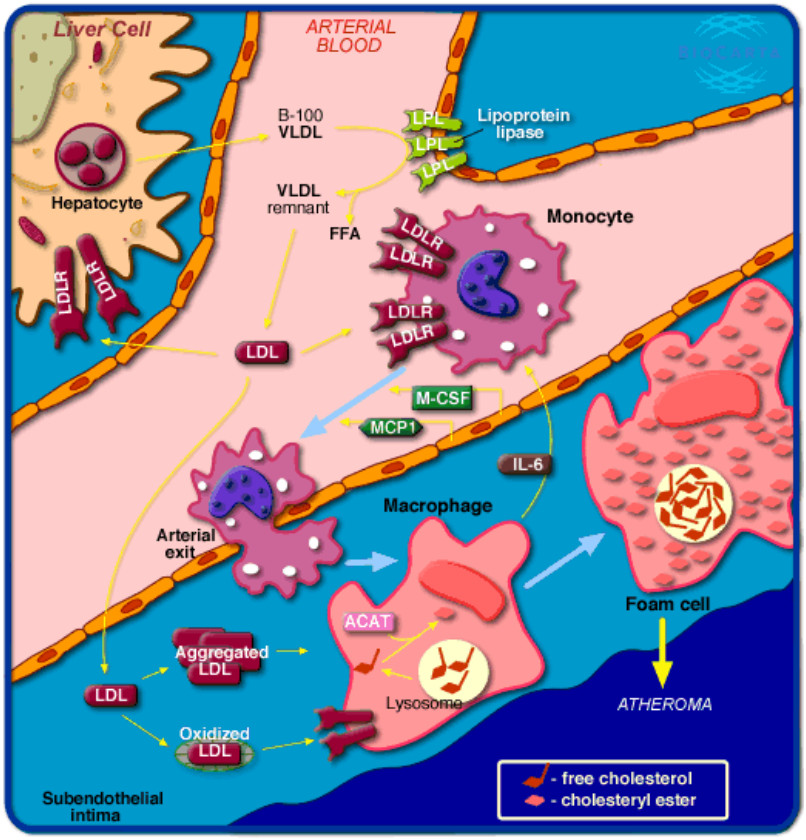
LDL particles contain a core of cholesterol esters and lesser amount of triglycerides ,and has an abundance of apo B-100 which serves as a ligand to bind to LDL receptors.LDL acts on hepatic and non hepatic tissues. In hepatic tissues, LDL is converted to bile acids and secreted into the intestinal lumen. In non hepatic tissues, LDL is used for hormone synthesis, cell membrane synthesis or stored as esterified fat.

The uptake of LDL intracellularly is controlled by the apoB/E LDL receptor expression by negative feedback mechanism(16).



Source :www.gbhealthwatch.com

When there is excessive of cholesterol, the receptor is down regulated. When the intracellular cholesterol decreases as expressed by a decrease in HMG Co A reductase, induces expression of LDL receptors leading to an increase in uptake.



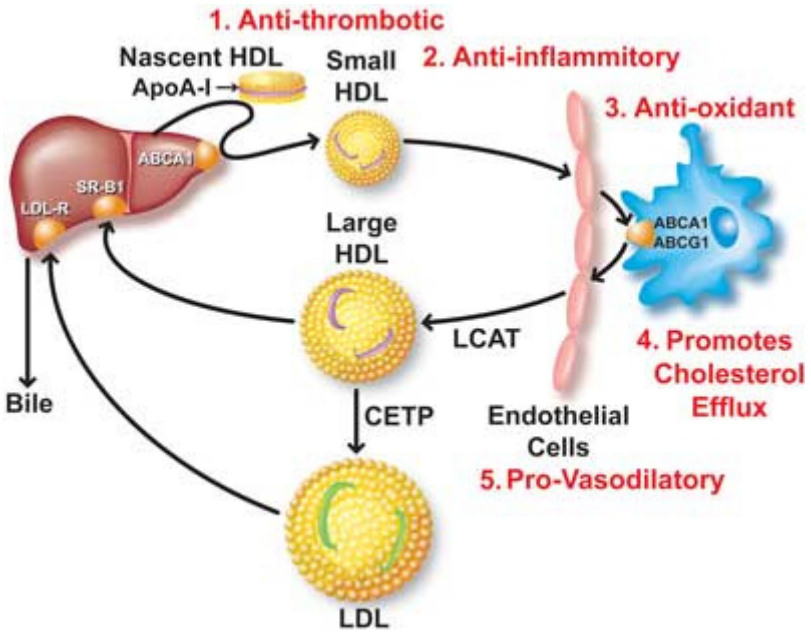
Source:www.biocarta.com/pathfiles

LDL can enter macrophages and other tissues by an unregulated scavenger receptor, leading to excess cholesterol within the cell, which forms foam cells .This predisposes to the formation of atheromatous plaques.

HDL (High density lipoprotein):

HDL is synthesised in the liver and intestine , composed of phospholipids and apolipoproteins. Triglyceride depleted VLDL and chylomicrons provide the necessary

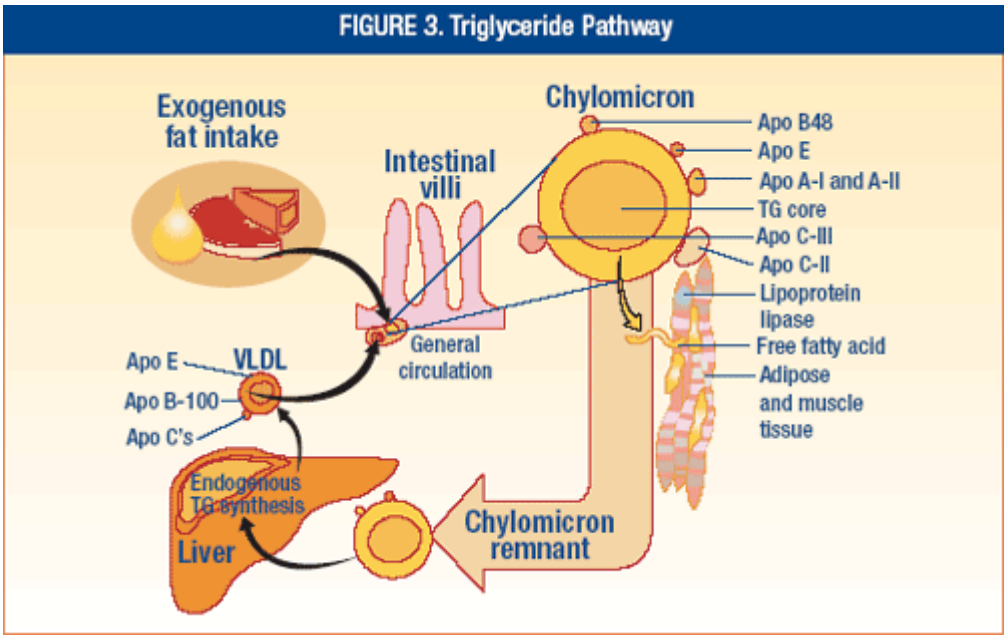
surface components like phospholipids, cholesterol and lipoproteins . Apolipoprotein A-I , on the surface of HDL serves to mobilise (unesterified) cholesterol from the tissues into the HDL particles by diffusion where it is esterified to cholesterol ester by LCAT , a plasma enzyme which is controlled by apolipoprotein A-I. HDL also accepts cholesterol released from lipolysis of triglyceride containing lipoproteins.



Source: www.aacc.org/publications

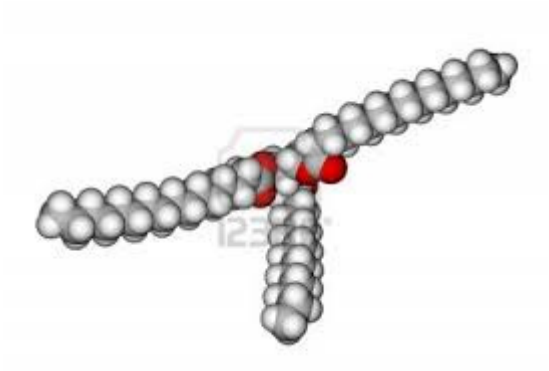
A cholesterol reflux regulatory protein plays a major role in the transfer of intracellular cholesterol to the cell membrane where it is taken up by HDL(17).CETP (Cholesterol ester transfer protein) aids in the take up of these newly formed cholesterol ester by the apoplipoprotein B containing lipoproteins like VLDL,IDL and LDL which is then utilised for steroid synthesis or for storage.

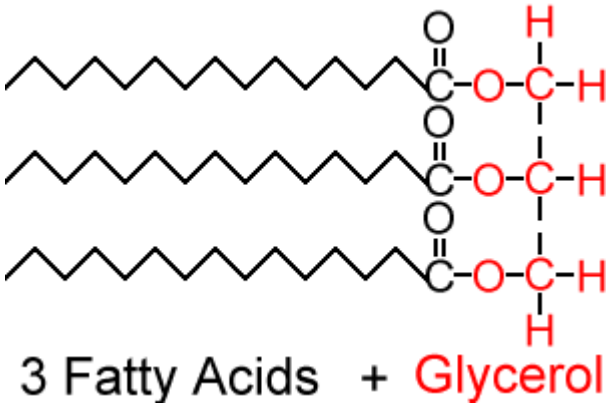
TRIGLYCERIDES:



Source : totalpict.com/elevated triglycerides in accutane.

Triglycerides are a group of lipids which contain a glycerol component esterified into 3 fatty acid chains.





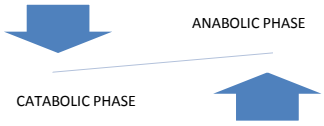
Source :www.123rf.com/triglyceride-optimised-molecular-structure

Each chain can be saturated or unsaturated depending on the single or double bonding of the carbon and hydrogen atoms within these fatty acid chains. Triglycerides are the most abundant form of lipids found in the diet. It is acted upon by pancreatic lipase in the gut, which hydrolyses one fatty acid chain to release 2 free fatty acids and one 2-Monoglyceride compound. In response to lipids in the meal, cholecystokinin is released which stimulates the release of bile salts into the duodenum. Bile salts combine with lipid molecules to form a hydrophobic core and a hydrophyllic surface. Absorption of these lipid particles takes place across the intestinal cell membrane by diffusion and also by the aid of lipid transporters. Once, inside the cell, the free fatty acids and 2-monoglyceride particle reach the endoplasmic reticulum to form triglycerides again , which are then packed in the golgi apparatus into chylomicrons .These chylomicrons reach the circulation and are taken up by the liver (18).

LIPIDS IN PREGNANCY

Pregnancy is a dynamic state in which Glucose, Free fatty acids, Long chain Poly unsaturated fatty acids(LCPFA) ,Amino acids , Minerals and Vitamins have to be continuously supplied to the fetus , inspite of intermittent food intake by the mother.

Pregnancy is divided into two phases:



Metabolic adaptations during pregnancy is essential :

1.To ensure adequate growth and development of the fetus.

2.To provide the fetus with adequate energy stores and substrates that are needed following birth.

3.To provide the mother with adequate substrates and stores to cope with the demands of pregnancy, labour and lactation.

One of the metabolic adjustments is the accumulation of fat deposits in the maternal tissues during anabolic phase.

ANABOLIC PHASE:

During anabolic phase, the number of insulin receptors on the adipocytes increase

⇩

Insulin sensitivity increases

⇩

Increased activity of Lipoprotein Lipase (LPL)

⇩

Increased hydrolysis of Triglycerides

⇩

Increased tissue uptake of lipids ⟹ Lipogenesis

There is increase in maternal fat deposition (3.5 to 6 kg increase in body weight).This is to mainly spare the glucose for the fetus during the catabolic phase.Lean women have a higher increase in fat stores more than obese women due to insulin sensitivity.

Important features of fat deposition during Anabolic Phase:

1.There is hyperphagia which increases progressively as gestational age increases.

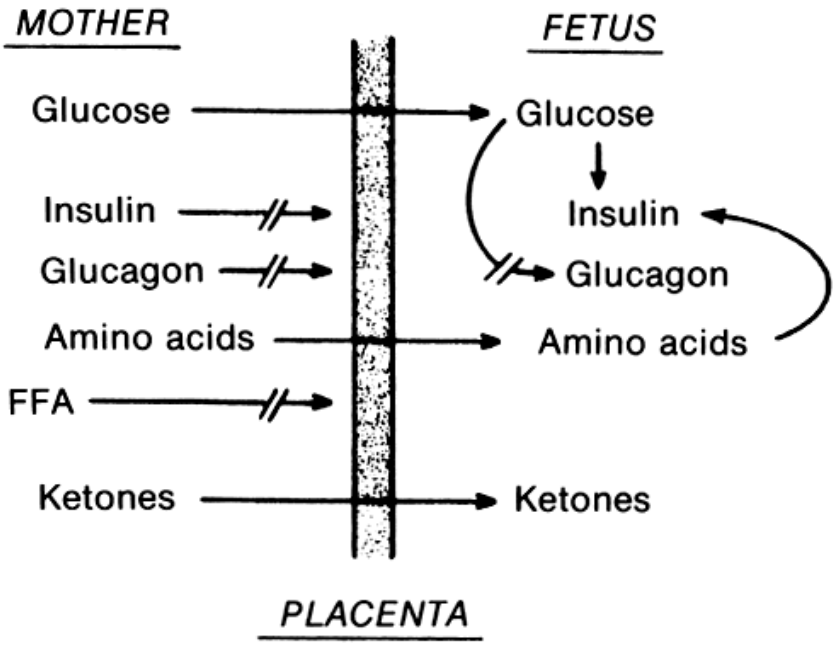
2.Promotion of lipogenesis and suppression of lipolysis mediated by progressive increase in insulin (in early pregnancy there is increased response of pancreatic β cells to increase in glucose)and it's sensitivity , enhanced by progesterone and cortisol.(19)

3. The proportional increase in adipose tissue Lipoprotein lipase activity (20–22)which hydrolyzes Triglycerides in the form of TG – rich lipoproteins, chylomicron and VLDL, which are converted to remnant particles and IDL.The hydrolytic particles ,Non esterified fatty acids and Glycerol are taken up by subjacent tissues(23).

4.The unique capacity of tissue to utilise intracellular glycerol released during lipolysis.

During the last trimester there is a change to catabolic state. Placental growth hormone, Human placental lactogen , Leptin and TNF-α cause insulin resistance. High levels of these placental hormones have a net lipolytic effect. Maternal fasting hypoglycaemia enhances release of excessive catecholamines, along with increased secretion of Human placental lipase , insulin resistance by placental hormones lead to the net breakdown of maternal fat deposits. Non esterified fatty acids (NEFA) and Glycerol are released as a result of the above mentioned lipolysis. These lipolytic products reach the maternal liver where they are converted into their active forms acyl

co –A and Glycerol-3 – phosphate which are then re esterified for the production of triglycerides which is then released into the maternal circulation. Acyl co-A can also be converted to acetyl co –A for producing energy and synthesis of ketone bodies. Glycerol is also used for producing glucose. Fetus uses glucose and amino acids maximally by 22-26 weeks which gradually decreases by third trimester by which time lipids are transported maximally for increasing the body weight. Hence the mother's glucose is spared .Ninety percent of fetal fat deposition (7g /day) takes place in the third trimester and human beings are born with the maximum percentage of fat 12-15 % compared to other animals.



Source:www.msdlatinamerica.com

During maternal fasting period, when the glucose is low, glycerol, released from lipolysis is utilised for gluconeogenesis(24).There is accelerated release of ketone bodies during this period . Ketone bodies support the fetus in 2 ways : 1. Ketones are used by the mother, glucose is spared for the fetus to utilise.2. Ketone bodies are

transferred efficiently to the fetal plasma where it is used as oxidative fuel and for the brain lipid synthesis.

The net breakdown of maternal lipids during the third trimester corresponds mainly to an increase in Triglycerides , mainly in the LDL and HDL fractions , compared to other phospholipids and cholesterol (21,25). Other hormones also contribute to maternal hyperlipidemia in third trimester.

Estrogen : 1.Increase in endogenous VLDL –TG(26).

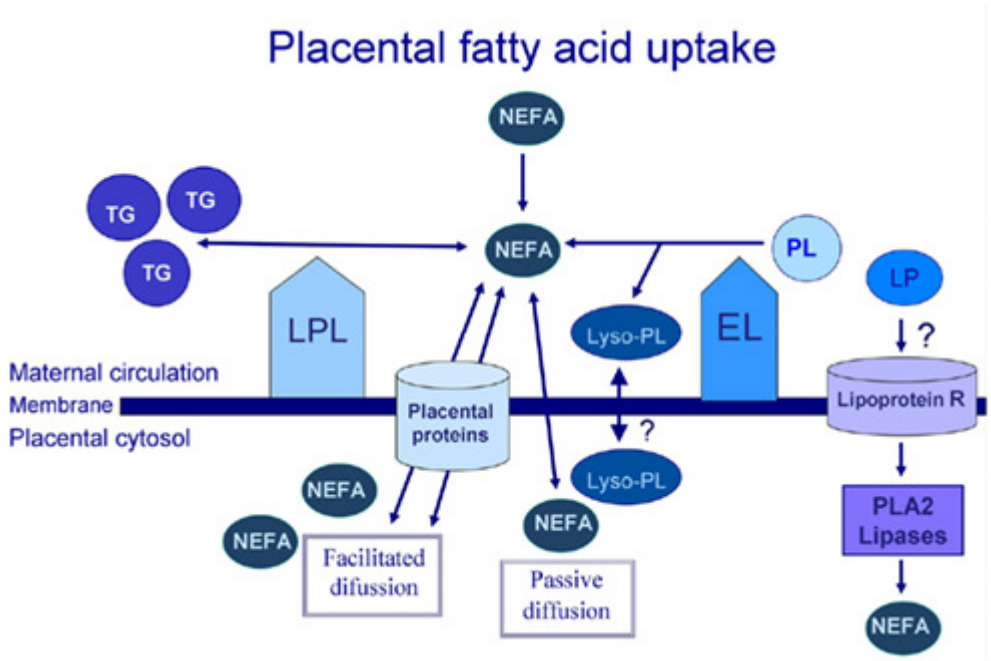
2.Decrease in adipose tissue Lipoprotein lipase activity(21,23).

3.Inhibition of hepatic triglyceride lipase activity(23).

Prolactin: Inhibits adipose tissue Lipoprotein lipase activity.

Hence the combined effect of enhanced liver production of VLDL-TGL, decreased removal from circulation due to decreased Lipoprotein lipase activity, increase in CETP activity and decrease in Hepatic lipase activity ,increase in insulin resistance , increase in estrogen activity all lead to the net increase in accumulation of triglycerides in the third trimester.

The lipoprotein Triglycerides do not directly cross the placental barrier.The lipoprotein TG are taken up by the placenta and transferred to the fetus as fatty acids by diffusion. The placenta selectively increases transport of essential Fatty acids and Long chain polyunsaturated fatty acids (LCPUFA) to the fetus. The Placental plasma membrane has fatty acid binding protein which preferentially uptakes only LCPUFA and transfers to the fetus. This is essential for fetal growth and nervous tissue development.



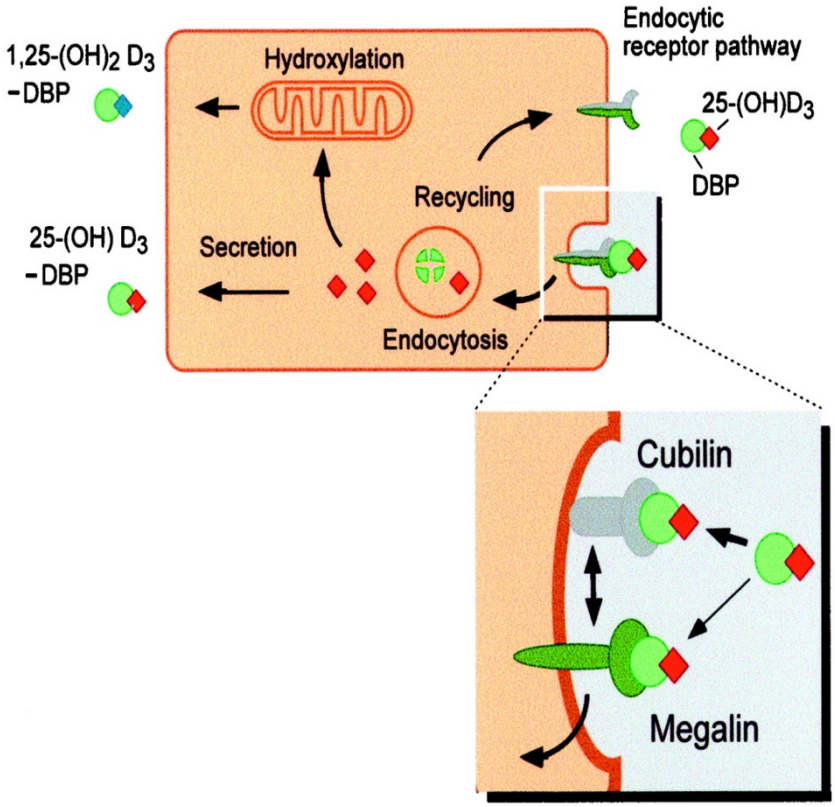
Source :www.frontiersin.org

Cholesterol is an essential component of cell membrane, precursor of bile acids and steroid hormones specially progesterone, precursor of oxysterol, is needed for cell proliferation and differentiation. Cholesterol also acts as a mediator of metabolism through propogation of signalling cascades. It is essential in the propogation of 'Sonic Hedgehog –SHH' signalling responsible for the development and patterning of the central nervous system(27–29). The average requirement of cholesterol per gram of body(fetal) tissue is 1.5 mg whereas per gram of brain tissue requires 7 mg, making a total requirement of around 8 gm for a 3.2 kg baby at term (30). The yolk sac and placenta play an important role in the feto maternal transfer of nutrients. The yolk sac develops after implantation of the embryo, by day 10 and slowly becomes non functional by the eighth week of pregnancy. The placenta becomes functional by the fourth week of pregnancy.

Cholesterol is made available to the fetus by the following ways: 1. Transfer from the maternal circulation. 2. Synthesis by the fetus.

Yolk sac :

The vitelline arteries and veins form the vasulature of the yolk sac and fuse with the fetal vessels within the developing embryo.

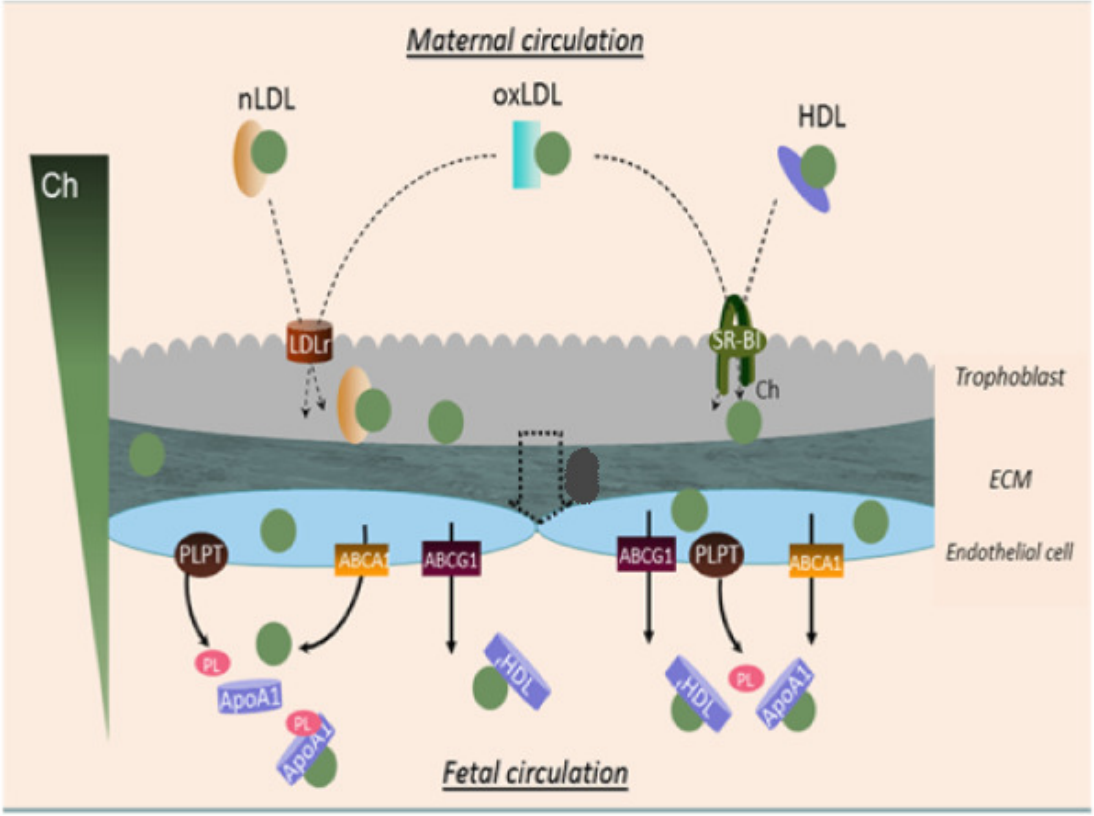


Source : www.pnas.org

The yolk sac contains Lipoprotein receptors like Megalin, cubilin and SR-B1 for apo B,E – containing particles and for HDL(31–34).The yolk sac is also capable of uptake of particles without a receptor –dependent pathway(31,35). The lipoprotein cholesterol is then hydrolysed to free cholesterol , synthesis of new lipoproteins takes place and secreted into the vitelline vessels.The visceral endodermal cells of the yolk sac like enterocytes and hepatocytes are also capable of secreting lipoprotein.

The placenta:

In the placenta, the maternal and fetal circulation are separated by a layer of multinucleated trophoblasts called the syncytiotrophoblast which forms a physical barrier. The trophoblasts are capable of taking up the cholesterol thro the lipoprotein receptors and also through receptor independent channels.



Source :intechopen.com

The lipoprotein receptors found in the placenta are:

(i)LDL receptor. (ii) VLDL receptor. (iii)Class A scavenger receptor .(iv) Class B scavenger receptors.The class A scavenger receptors are ; LDL –receptor related proteins, the apolipoprotein E receptor 2, megalin and cubilin .VLDL and LDL are taken up by apo E,B receptors .HDL is taken up by SR-B1 receptors. The VLDL,

LDL and HDL particles are then taken up by the lysosomes where they are hydrolysed and then effluxed thro the basolateral membrane of the trophoblasts into the fetal circulation. Around 20 % of the sterol used by the fetus is from the maternally derived placental cholesterol.

When the mother has low cholesterol levels as seen in abetlipoproteinemia , hypobetalipoproteinemia, low cholesterol diet, it does not affect the growing embryo. This is because ,placental sterol synthesis increases to compensate for the decrease in transfer from maternal circulation(36–38).When the mother has high cholesterol , as normal physiological change, familial hypercholesterolemia, obesity and overt diabetes mellitus, the fetus responds by formation of fatty streaks in the fetal aorta which can predispose to atherogenesis later on in life. If adequate maternal cholesterol is not available , fetus tends to be smaller and microcephaly can occur as seen in Smith –Lemli-Opitz Syndrome.

In non pregnant state, higher concentration of VLDL-1 is seen in the immediate post absorptive state, failure of action of insulin and associated with increased risk of Coronary heart disease.The concentration of VLDL-2 , precursor of IDL and LDL does not change drastically. In pregnancy, though the concentration of triglycerides increased, the ratio of VLDL1:VLDL2 remained constant(23). Even though the later part of pregnancy has altered lipid and lipoprotein levels, the hyperlipidemia seems to be 'balanced'.

During normal pregnancy , plasma TG increase by 200-400%, cholesterol by 25-50 % ,total LDL mass by 70 %.The lipids are enriched with Triglycerides and depleted of cholesterol.

Though the hyperlipidemia of pregnancy is termed 'physiological', it is influenced by genetic factors, pre existing medical conditions, medical complications of pregnancy and other maternal factors.

MATERNAL FACTORS:

1.Obesity

2.Maternal weight gain during pregnancy.

3.Maternal nutrition.

4.Pre pregnancy lipid levels.

PRE EXISTING MEDICAL CONDITIONS:

1.Type I /II Diabetes Mellitus.

2.Hypothyroidism.

3.Hypertension.

4.Renal diseases.

5.Alcoholism.

6.Medications (LMWH,Glucocorticoid)

MEDICAL COMPLICATIONS OF PREGNANCY:

1.Pre-eclampsia.

2.Gestational Diabetes Mellitus.

3.IUGR

Physiological hyperlipidemia, out of proportion can also lead to cholesterol gallstones, intrahepatic cholestasis, acute pancreatitis and Endothelial dysfunction.

Failure to develop normal hyperlipidemia in pregnancy can lead to IUGR and future development of metabolic syndrome.

As seen earlier, there is increased concentration of VLDL-1 TGL during pregnancy.VLDL is a major precursor of LDL and reflects on the circulating TG levels. These LDL particles undergo a reduction in the size by the action of hepatic lipase and become small , dense LDL subfractions. These small dense LDL particles remain in the circulation for a longer period of time as they do not readily bind to their receptors. They have a better capacity to penetrate the arterial intimal layer, easily oxidised (due to less concentration of vit E and other antioxidants).They are taken up by macrophages to form foam cells which initiates atherogenesis. So , the question arises, whether normal pregnancy is atherogenic ?

Though hypercholesterolemia is transient and limited to pregnancy, it triggers fatty streak formation in the fetal aorta which influences atherogenesis later in life(8).Autopsy studies revealed that offsprings (between ages of 1-13 who died of trauma or other causes) of hypercholesterolemic mothers developed atherosclerosis much faster with 1.5 to 3 times larger lesions than offsprings of normocholesterolemic mothers as described by FELIC study (Fate of early lesions in Children study)(39).

Umbilical cord blood samples from normal pregnancy showed a higher level of HDL and a lower LDL :HDL ratio as compared to the maternal blood indicating that the fetus is protected against atherogenic lipoprotein(40).

Lipids in pre eclampsia:

Pre eclampsia is a specific vascular disorder unique to human pregnancy.It is a major cause for maternal and fetal morbidity and mortality.It is associated with placental dysfunction, oxidative stress ,endothelial cell activation and dyslipidemia. Dyslipidemia as characterised by increased TG levels , reduced HDL levels and increase in smaller, dense LDL (41).The risk of pre eclampsia increases significantly with associated conditions like Diabetes mellitus, chronic hypertension, thrombophilias and renal diseases , all of them have vascular endothelial dysfunction(42) .

In pre eclampsia, there is reduced placental perfusion, acute atherosis in decidual vessels as shown by accumulations of foam cells and perivascular mononuclear cell infiltration. Triglycerides increase two fold compared to normotensive women. Though the TG are high, effective transfer to the fetus is altered due to placental dysfunction. As mentioned earlier, maternal TG cannot cross the placental barrier. It has to be hydrolysed into Free fatty acids by the human placental LPL which is subsequently transported to the fetus. In umbilical cord blood samples of babies born to pre eclamptic mothers, higher TG, higher LDL:HDL ratio and lower HDL was found.LPL expression was also enhanced in pregnancies with pre eclampsia and IUGR suggesting that adaptive mechanisms are at play to overcome the uteroplacental insuffiency and to ensure steady supply of fatty acids to the fetus.

Serum triglycerides and VLDL was found to be significantly higher in women with pre eclampsia than normotensive women(43).Women with elevated triglyceride levels had twice the risk of developing pre eclampsia than women with normal values(44). In

another study, triglycerides measured at 28-32 weeks was most predictive of developing pre eclampsia later during the gestation(45).

In IUGR, there is decreased concentration of Total cholesterol, triglycerides, VLDL and LDL leading to decrease in transfer of Glycerol, LCPUFA and essential fatty acids to the fetus(46).

Lipids and infant birthweight:

In 2011, Vinod.K.Misra studied the influence of variation in maternal serum lipid levels on variation in birthweight in obese and normal weight women. In obese women, they found a significant inverse relationship between HDL and birthweight of the fetus. Infants born to overweight or obese women had a significantly higher birthweight than infants born to normal weight mothers. In overweight mothers, 13 gms decrease in birthweight was associated with 1mg/dl increase in maternal HDL concentration .In normal weight mothers, 6.4 gms decrease in birthweight was associated with 1mg/dl increase in maternal HDL.HDL has anti oxidant and anti thrombotic properties which influences placental circulation and fetal growth. Reduction in the circulating level of HDL may be associated with placental vasculopathy and increased risk of pre eclampsia(47).

In 2001, Kitajima et al found that hypertriglyceridemia at 24-32 weeks of Gestational age was a significant predictor of having a large for gestational age baby at term independent of maternal glucose levels, obesity, pre pregnancy weight and weight gain during pregnancy(48).

In 2002,Haggarty P et al postulated that >90 % of fat deposition in the fetus occurs in the last 10 weeks of pregnancy. Fetal blood is enriched with LCPUFA relative to

maternal supply. The placenta regulates it's own Fatty acid substrates supply via the placental leptin on maternal adipose tissue. Fatty acids cross the microvillous and basal membranes by simple diffusion and by the action of membrane bound and cytosolic Fatty acid binding proteins. The direction and magnitude of fatty acid influx is dictated by the relative abundance of fatty acid binding sites. The placenta selectively transports important LCPUFA to the fetus by 1.Selective uptake by syncytiotrophoblast. 2.Intracellular metabolic channelling of individual fatty acids.3.Selective export to fetal circulation. Most of the LCPUFA accumulated by the fetus is stored in the adipose tissue for use in early post natal life(6).

In 1999, Sattar et al, found that median cholesterol, LDL, IDL values were lower in women with IUGR. One of the reasons being, these women had a low cholesterol in the first trimester itself. Normally there is a 60 % increase in mean cholesterol levels, mainly LDL by 35 weeks. When there is a failure in the above mentioned increase, either due to increased degradation of LDL or decreased synthesis of LDL, IUGR ensues(49).

In pregnancies complicated by pregestational diabetes, gestational Diabetes mellitus and IUGR, there is an impaired transfer of LCPUFA from the mother to the fetus(50).There has been reports of normal LCPUFA concentration in the mother's erythrocytes and plasma phospholipids but reduced in the plasma phospholipids of the neonate(51–53).This may explain the delayed brain maturity, altered behavioural and intellectual development of the children , shorter attention span and motor dysfunction at school age of children born to mothers with pregestational Diabetes or gestational Diabetes mellitus(54).

In another study, in which lipids and lipoproteins were compared between normal pregnancies and pregnancies with ultrasound proven Intrauterine growth restriction, they that Triglycerides, VLDL, LDL and Total cholesterol increased gradually with gestational age , in normal pregnancies. Whereas in pregnancies with IUGR, all the above were found to be decreasing with advancing gestation.HDL did not show any significant change. Serum cholesterol and LDL was found to be significantly lower in women with IUGR babies(55).

In a population of well controlled GDM pregnancies, circulating maternal lipids, and not glucose , correlated with weight of the fetus in the third trimester. Maternal free fatty acids and glycerol , measured close to term correlated with Large for Gestational Age fetus, than the mother's BMI. In Small for gestational age babies, TG was high due to decreased adipose tissue mass leading to decrease in LPL activity. In LGA babies,high free fatty acids,high insulin to glucose ratio (suggestive of in utero insulin resisitance) and low TG levels were found(3).

In 1999,Patrizia et al carried out a study to investigate the changes in circulating lipids and lipoproteins in normal and pregnant women. Triglycerides, LDL and Total cholesterol were significantly higher in pregnant women than non pregnant state. Changes in LDL during pregnancy might be used to identify women who would later develop atherogenic small dense LDL to different stimuli , later in life(56).

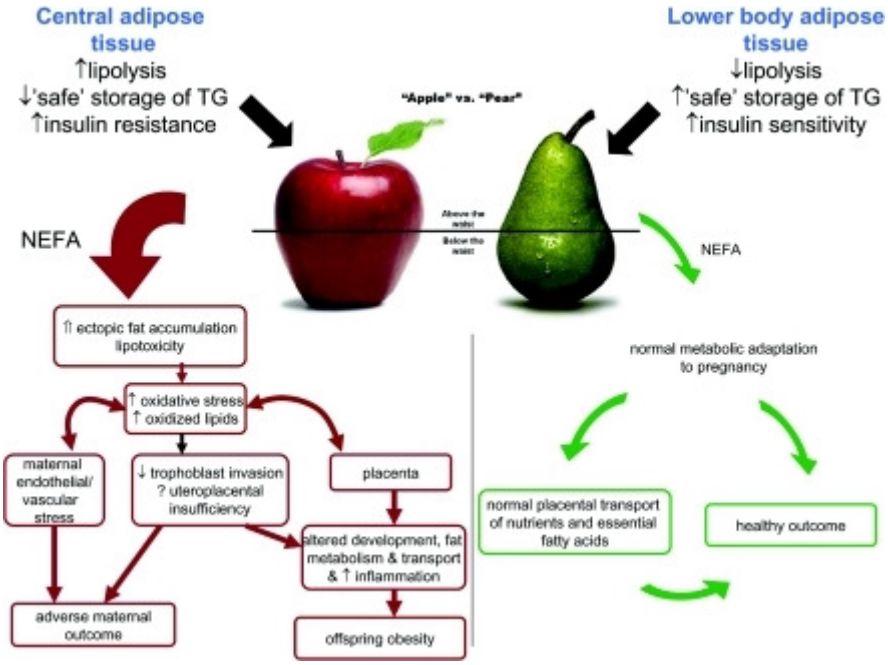
In 1997, Sattar et al studied 12 pregnant women to see the pattern of changes in the lipoprotein fractions throughout pregnancy. He found that there was a certain threshold in Triglyceride level beyond which appearance of atherogenic small dense LDL –III particles accelerated.LDL-I increased by 2 fold, LDL-II by 40 % and LDL –

III increased 4 fold. This alteration in the increase of LDL-III was highest in women who had the highest triglyceride level at 10 weeks of gestation(23).

In 2001,Sandra et al studied 250 pregnant women, to investigate the impact of three Lipoprotein lipase polymorphisms & apoE genotypes on lipid levels in pregnancy. They found that S447X carriers had lower TGL,N291S carriers had lower HDL . The E2 allele was associated with lower TC,LDL compared to E3/E3 genotype. They concluded that severe triglyceridemia in late pregnancy is due to genetic mutations in genes of lipoprotein lipase or ApoE (57).

In 1995, Nolan et al studied 388 pregnant women to identify the values of triglyceride measured earlier in pregnancy that will predict the development of Gestational Diabetes mellitus later in pregnancy. They found that Triglycerides measured between 9-12 weeks correlated significantly with developing GDM later in pregnancy , more in Asian born women (3 times) than Caucasian women. Triglycerides correlated positively with birth weight ratios of babies born, more in Asian women than Caucasians(58).

Maternal weight and Lipids:



In 2010, Vahratian et al , studied the effect of maternal pre pregnancy overweight and obesity on variation in lipid profile during pregnancy. They found that rate of change in LDL cholesterol and total cholesterol levels were lower in obese and overweight women than their normal weight counterparts. They speculated that the differences was due to metabolic dysregulation in overweight and obese mothers leading to adverse effects on the fetus as well(12).This is due to reduced action of hepatic triglyceride lipase activity which is responsible for converting the larger buoyant LDL subclasses containing more of cholesterol to smaller, dense LDL particles with more triglyceride content , as pregnancy advances. In non pregnant state, such a shift to triglyceride rich LDL particles is associated with atherogenesis, metabolic syndrome and diabetes. It is also considered as a systemic marker for low grade inflammation and vascular adhesion molecules(59).This shift to triglyceride rich LDL in overweight and obese women may also explain the increased risk of pre eclampsia in such women(60).

Almost two in three women in the reproductive age group are overweight or obese(61). Metabolic changes in obese women may predispose to metabolic and cardiovascular diseases later in the life of the fetus(62).The complications of maternal obesity is mostly related to the pre pregnancy weight than the weight gain during pregnancy or the weight at term.The average weight gain recommended in pregnancy is as follows(63):

Pre pregnancy BMI	Recommended weight gain
< 19.8	12.5 -18.0
19.8 – 26.0	11.5-16.0
>26.0-29.0	7.0-11.5

It was found that lean women gained a greater percentage of fat during pregnancy, more in peripheral tissues (biceps and triceps area) than obese women(64).Increased incidence of diabetes and increasing maternal BMI has been associated with infants born with a birth weight greater than 90 th percentile (>4 kg)(65).Children born to obese mothers were twice likely to be obese by 2 years of age. If the mother had a BMI > 30 in the first trimester, the prevalence of childhood obesity (BMI >95 th percentile), at 2 years was 15.1 %, 3 years was 20.6 % and at 4 years , was 24.1 %.This was 2.5 times more than the obesity seen in children born to normal weight women(66).

In women with positive screens for Gestational diabetes , but with normal glucose tolerance tests, maternal pre pregnancy BMI and triglycerides measured in the third trimester correlated significantly with infant birth weight (67).

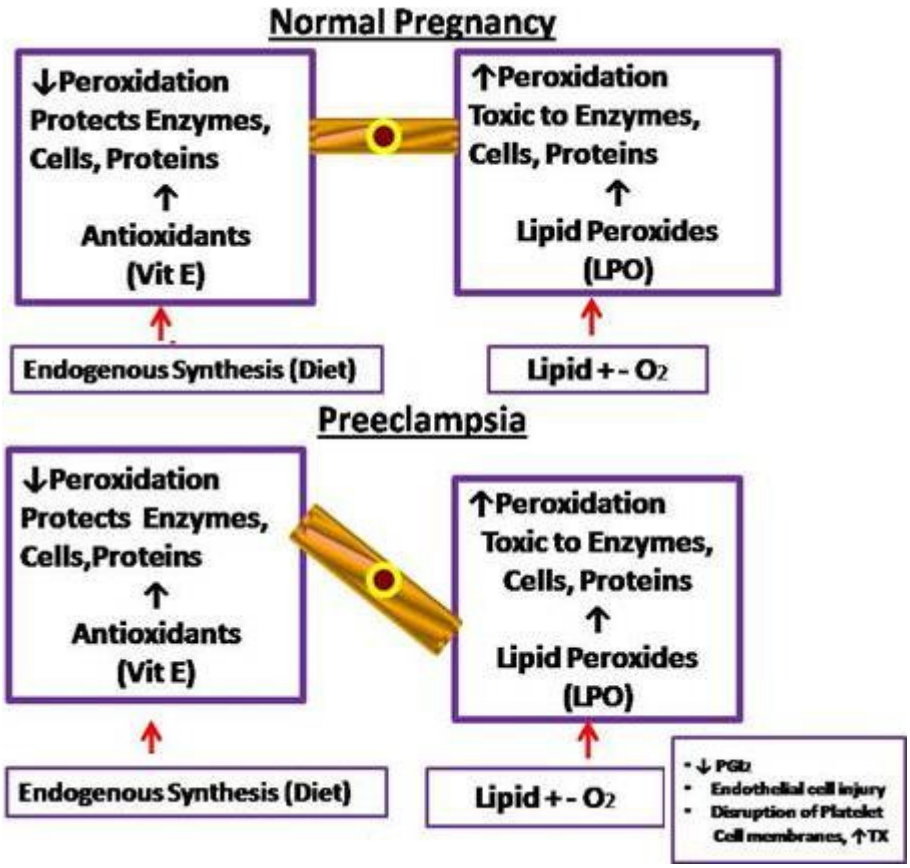
In another study ,maternal adiposity, pre pregnancy BMI and weight gain during pregnancy were found to be the strongest predictors of infant birthweight, more in the large for gestational age babies. Obesity in the mother is usually associated with chronic inflammation (increased CRP levels) and adipocyte dysregulation (increased leptin and low adiponectin levels). Leptin and C-reactive protein correlated negatively with infant birth weight(68).

Lipids and timing of delivery:

In a study by Mudd et al, they found that extremely low total cholesterol, HDL and LDL was aasociated with an increase in the risk of medically indicated preterm delivery (as in pre eclampsia).High total cholesterol, LDL and triglycerides were associated with an increase in the risk of having spontaneous preterm delivery(11).

Lipid profile and adverse pregnancy outcomes:

In a study, with data derived from Amsterdam Born Children and their Development cohort, fasting lipid profile in early pregnancy was correlated with the incidence of adverse pregnancy outcomes like Gestational hypertension, pre eclampsia, Small for gestational age babies, Large for gestational age babies, Pre term labour and fetal loss. They found that , for every unit increase in triglyceride taken in the first trimester , there was a significant increase in the risk of developing gestational hypertension, Pre eclampsia and induced pre term labour. Total cholesterol was not associated with adverse outcomes(69).



Source :www.pharmainfo.net

The probable explanation being, elevated triglycerides in the early gestation may induce endothelial dysfunction. There is increased peroxidation of these lipids ,leading to oxidative stress releasing free radicals and lipid peroxides(70). These lipid

peroxides are toxic compounds that cause damage to endothelial cells(45).Hence , an elevated triglyceride can cause damage to the developing placenta (at the time of angiogenesis) , leading to future placental vascular damages as seen in gestational hypertension, pre eclampsia and Intra uterine growth restriction.

LONG TERM CHANGES IN LIPIDS (AFTER PREGNANCY):

Lipid profile values reach their peak by 31-36 weeks of gestation. The percentage of increase from early gestation is as follows(71,72):

LIPIDS	% OF INCREASE
Total cholesterol	43-53 %
LDL	36-40 %
HDL	0-25 %
TRIGLYCERIDES	150-230 %

After the delivery, total cholesterol and LDL cholesterol remain above the pre pregnancy values. Triglycerides fall rapidly. HDL remains lower than the pre conceptional value. These changes remain for several months , even up to an year(72,73).

Prior studies have found an inverse relationship between increasing parity and lower HDL levels(74,75). The Coronary Artery Risk Development in Young Adults (CARDIA) study, showed a decline in HDL for 2 years following the first birth , but not for further pregnancies(76).In another study , examining the lipid changes in Black and White women, HDL values declined to -4 to -5 mg/dl after the first birth. In women who were already parous, there was no significant fall in HDL after multiple births. This proves that fall in HDL is maximum after the first birth and the effect persists much longer. Low HDL cholesterol (<40 mg/dl) is a strong independent

predictor of developing coronary heart disease(77). There is a 2-3 % decrease in the risk of developing coronary heart disease for every 1 mg/dl increase in HDL cholesterol(78). A 10 % decrease in HDL cholesterol over 12 years leads to an increase in the risk of coronary heart disease by 10 %(79). Hence a 6 % decrease in the HDL levels , post delivery may increase the risk of coronary heart disease by 6 – 12 %.

In another study by Mankuta et al, Lipid profile was studied prior to, during , after and in subsequent pregnancies. They found :

LIPIDS	I TRIMESTER	II TRIMESTER	III TRIMESTER	POST PARTUM
Total cholesterol	Decrease of 11.4 mg/dl	Increase of 50.5 mg/dl	Increase of 28.5 mg/dl	In 1 year, returns to pre pregnancy level
LDL Cholesterol	Decrease by 3.3 mg/dl	Increase by 25.9 mg/dl	Increase by 19.4 mg/dl	Ist year returns to pre pregnancy values,further declines in 2^{nd} and 3^{rd} yr
Triglycerides	Decrease of 13.3 mg/dl	Increase by 64.9 mg/dl	Increase by 52.2 mg/dl	
	No change	Increase by 14 mg/dl	Decrease by 5 mg/dl	Levels plateau after first birth

The initial fall in the lipid profile values in the first trimester may be explained by the decrease in food intake due to the nausea and vomiting in the first trimester experienced by most of the women(21).

MATERIALS AND METHODS

TYPE OF STUDY : Prospective Observational Cohort study.

Scheme of research:

Pregnant Women aged between 20-35 years, with singleton pregnancy attending antenatal OPD in CMC Obstetrics department were recruited in the first trimester and followed up just after delivery. Morning fasting venous sample for lipid profile was collected in each trimester .Each sample was analysed for Total cholesterol, LDL, Triglycerides and HDL .Age, Socio economic status, Diet [vegetarian/non vegetarian], Pre pregnancy BMI ,blood pressure, fasting sugars ,Oral glucose tolerance test, weight gain in pregnancy, mode of delivery, incidence of adverse outcomes such as gestational hypertension and gestational diabetes mellitus, are the other parameters which were observed. Variations in Total cholesterol, LDL,HDL and Triglycerides between each trimester were analysed .Birth weight of the infants born to these women was recorded .

Inclusion criteria:

- Pregnant women aged 20-35 years residing in Tamil Nadu/Andhra Pradesh.
- Singleton viable pregnancy as confirmed by first trimester dating ultra sound.
- Willing to participate in the study with informed consent and deliver in CMCH .
- No prior history of chronic hypertension,diabetes mellitus and hypothyroidism.

Exclusion criteria:

- Multiple pregnancy.
- Women with prior chronic hypertension,diabetes mellitus and hypothyroidism.
- Who will not follow up in CMCH till delivery.

Variables analysed:

1.Lipid profile :Non pregnant values

Total cholesterol <160 mg/dl[optimal]

160-240 mg/dl [desirable]

>240 mg/dl[high]

LDL-C <100 mg/dl[optimal]

100-129[above optimal]

130-159[borderline]

160-189[high]

HDL-C >50 mg/dl [negative risk factor]

<40 mg/dl[risk factor]

Triglycerides <150 mg/dl[optimal]

200-499 mg/dl[high]

>500 mg/dl[very high]

Lipid profile analysis was done in the Biochemistry department by the following methods

Cholesterol: (CV of total chol testing -2.2%) Endpoint enzymatic colorimetric assay with cholesterol esterase, cholesterol oxidase and peroxidise in Roche P800 auto analyser.

HDL: (CV of HDL testing-2.8%) Colorimetric end point , enzymatic, anti b-lipoprotein antibody in Roche P800 auto analyser

LDL: (CV for LDL testing 6 %) Differential solubilisation with no pre treatment, end point enzymatic colorimetric assay, with cholesterol esterase ,cholesterol oxidase and peroxidise in Roche P800 auto analyser.

Triglycerides: (CV of Triglyceride testing-3.5%) Colorimetric,enzymatic,end point lipase,glycerokinase,glycerol phosphate ixidase , peroxidase, in Roche P800 auto analyser.

2.Socioeconomic status: Modified Kuppuswamy scale (2005)

A	**EDUCATION OF HEAD OF HOUSEHOLD**	**SCORE**
	Professional degree	7
	Post graduate & above,BA or B.Sc degree	6
	Intermediate or post high school diploma	5
	High school certificate	4
	Middle school completion	3
	Primary school or literate	2
	Iliterate	1

B	**OCCUPATION OF THE HEAD OF THE HOUSEHOLD**	**SCORE**
	Professional	10
	Semi professional	6
	Clerk, shop owner,farmer	5
	Skilled labourer	4
	Semi skilled labourer	3
	Unskilled	2
	Unemployed	1

C	**PERCAPITA INCOME(Rs per month) 2005**	**SCORE**
	>17,520	12
	8760-17515	10
	6570-8750	5
	4380-6560	4
	2628-4370	3
	885-2620	2
	<876	1

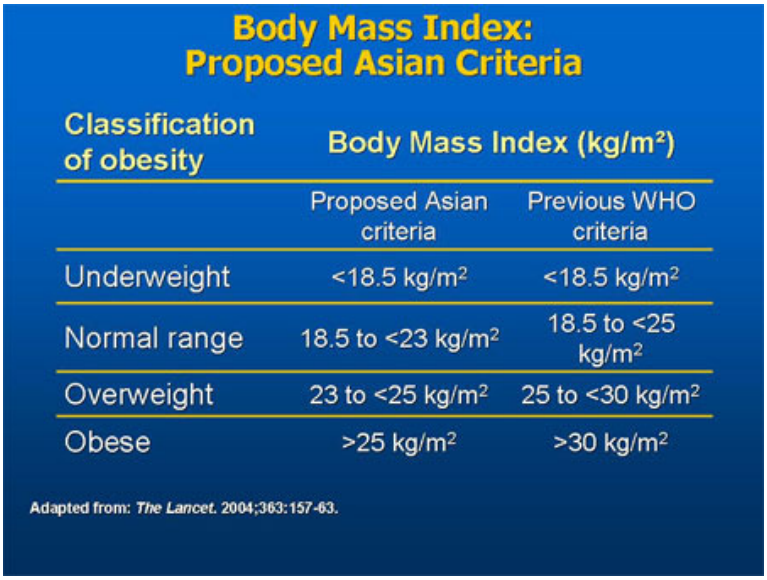
Total score	SES category
26–29	Upper
16–25	Upper middle
11–15	Lower middle
5–10	Upper lower
Below 5	Lower

SES - Socioeconomic status

3.BMI:

BMI: weight in kgs/height in cms2 .

Height as measured in cms by a wall mounted stadiometer. Weight as measured in Kilograms by bathroom weigh scale.



4.Blood Pressure: Checked in each trimester, Right arm sitting position by a manual sphygmomanometer.

5.Diet: Vegetarian /Non vegetarian.

6.Birthweight of the fetus: Checked at birth, expressed in grams.

7.Gestational Hypertension: Defined as increase in Blood pressure >140/90 mmHg on two occasions, 6 hrs apart detected after 20 weeks of pregnancy.(80)

8.Gestational Diabetes Mellitus: fasting blood sugar ≥ 92 mg % at any gestational age.

24-28 weeks, 75 gm Oral Glucose Tolerance Test (GTT), atleast one value abnormal,(fasting ≥ 92 mg/dl or 1 hr ≥ 180 mg/dl or 2 hr ≥153 mg/dl)(81)

9.Mode of delivery: Normal /Instrumental/LSCS.

SAMPLE SIZE CALCULATION

Sample size was calculated using the soft ware nMaster 2.0.The formula is "Hypothesis testing of two means" Based on the study by Retnakaran et al on the "effect of maternal weight,adipokines,glucose intolerance and lipids on infant birth weight among women without gestational diabetes mellitus", Research article in CMAJ ,May 2012.Triglycerides were significantly associated with changes in birth weight(68).

Standard Deviation in Group I (Low Birth weight)= 0.72

Standard Deviation in Group II(High Birth weight)=0.66

Mean difference in Triglycerides between the 2 groups= 0.24

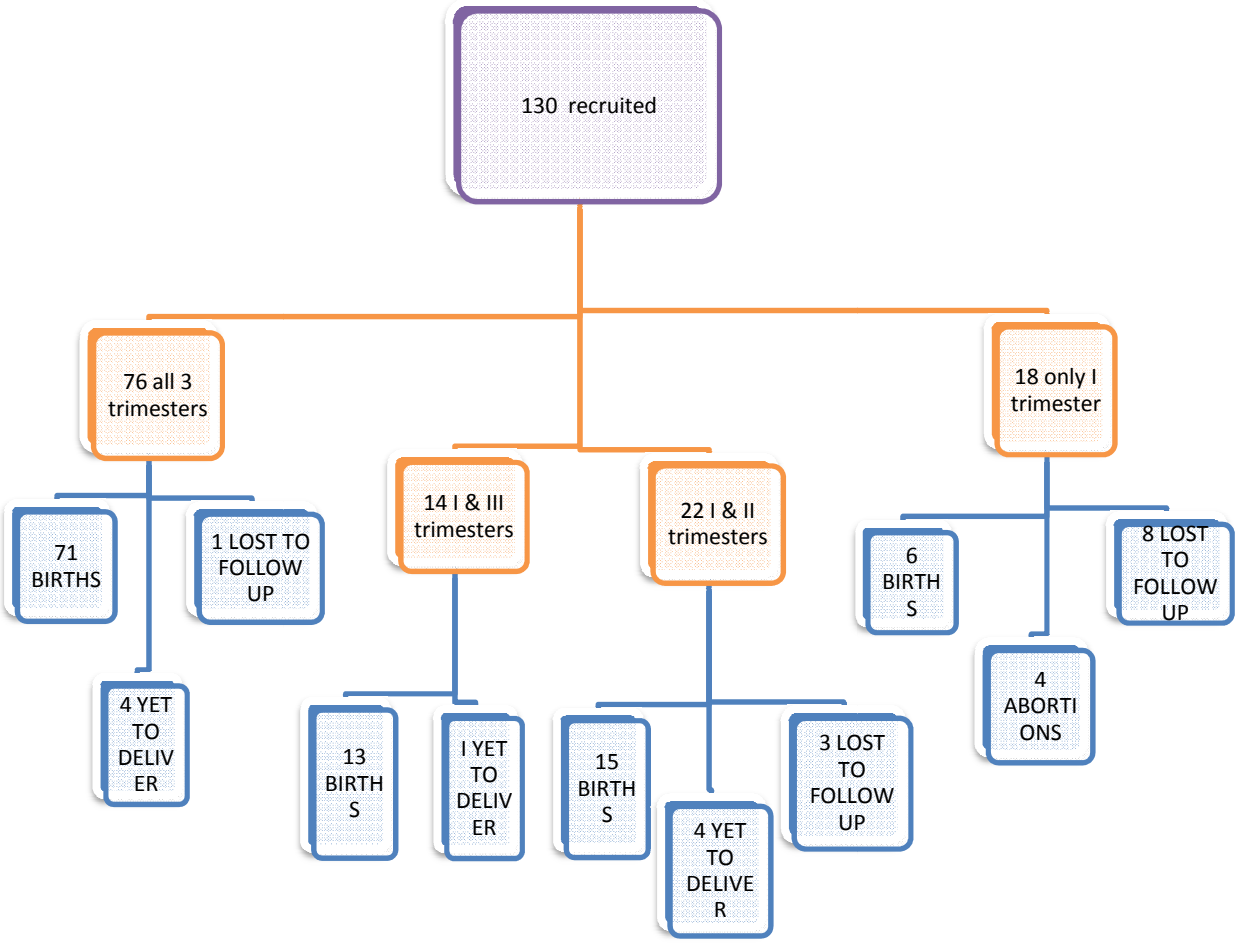
With an alpha error of 5 % and power of 80%, the sample size is 130

Time period : January 2013 –November 2013

Number recruited :130

RESULTS AND ANALYSIS

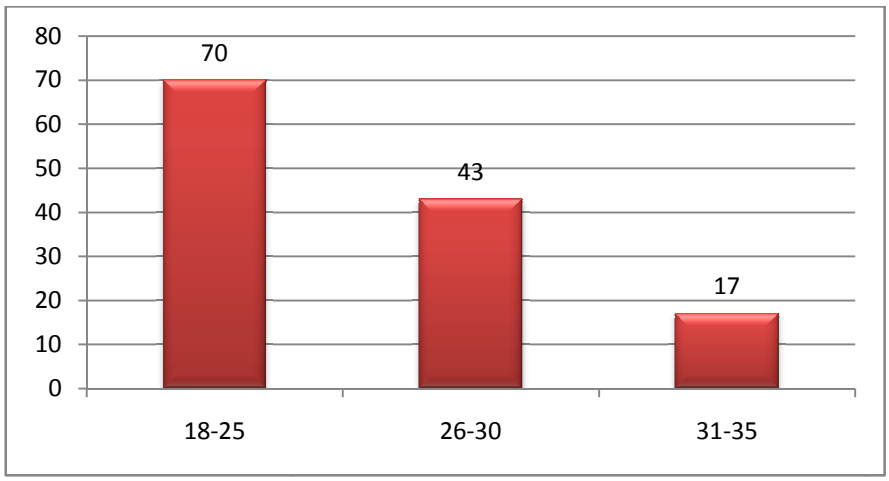
Figure 1.Overall distribution between three trimesters:



One hundred and thirty women were recruited after informed consent. Out of 130, only 76 women were able to give their blood samples in all three trimesters. Out of the 76, only 71 women had delivered within the time period of the study, 4 women were

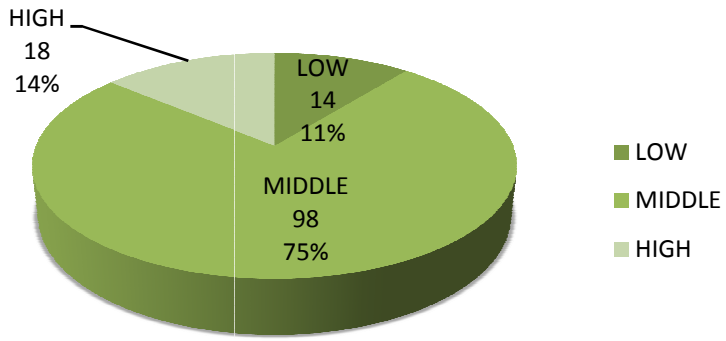
yet to deliver and 1 woman was lost to follow up. Follow up details of all the other recruited women is shown in figure 1.

Figure 2.Age distribution:



The age distribution among the women recruited is shown in figure 2 . Most of them are in the reproductive age group of 18-30 years.

Figure.3 Socio economic status:



Socio economic scoring (SES) was performed with the Modified Kuppusamy scale. Seventy Five percent (N=98) belonged to the middle SES strata, fourteen percent (n=18) were in the high SES class and eleven percent (n=14) were in the low SES class.(Figure 3)

Figure.4 -Parity:

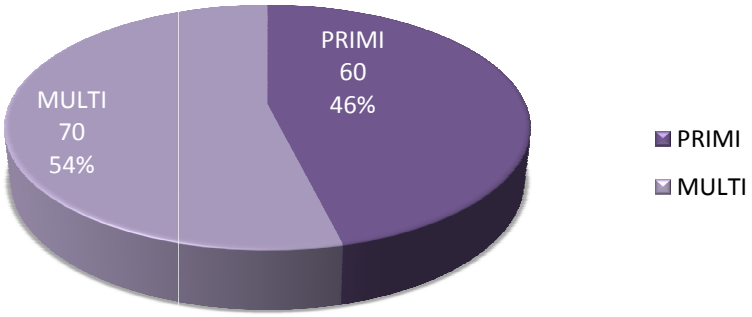


Figure .4 shows the obstetric score of the enrolled patients. Fifty four percent (n=70) were multigravidas and 46 % (n=60) were primigravidas.

Figure .5 -Diet :

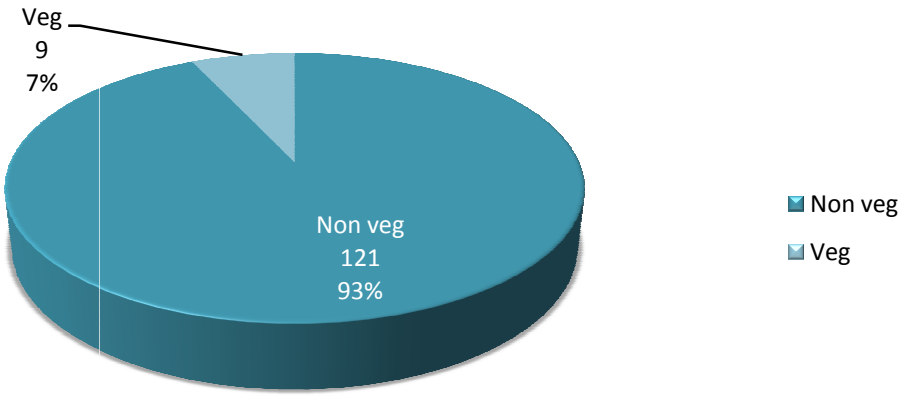


Figure.5 shows the diet distribution. Most of the women recruited were non vegetarians (93 %)

Figure.6 -BMI Distribution (I trimester) :

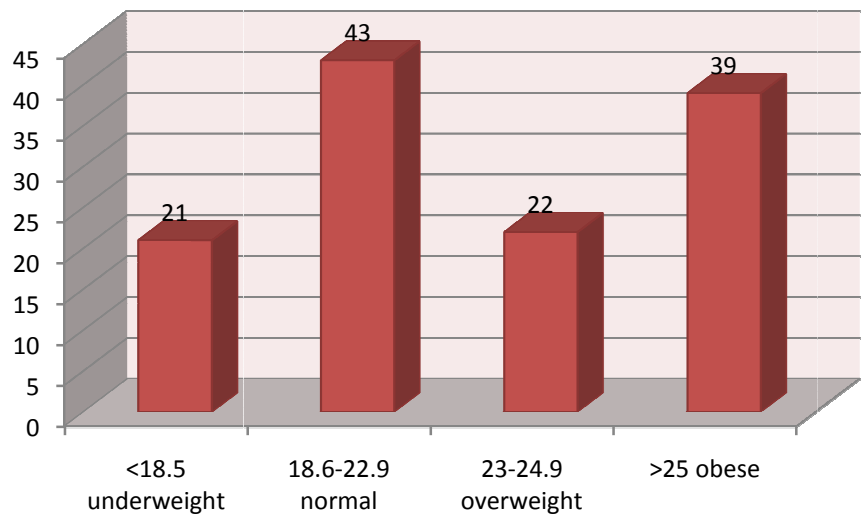
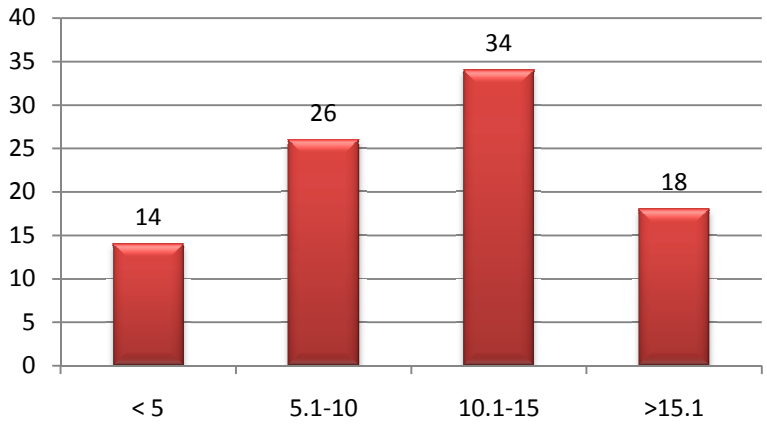


Figure.6 shows the Body Mass Index (BMI) distribution as measured in the I Trimester. BMI was within the normal range in 33 % , 16 % (n=21) were in the underweight group , 17 % (n=22) were in the overweight group, 31 % (n=39) were in the obese group .Baseline anthropometric values were missing for 5 women.

Figure.7-Weight gain in pregnancy(in kilograms):



Thirty six percent (n=34) of the women had a weight gain between 10-15 kg in pregnancy, 28 % had a weight gain of 5-10 kilograms, 19 % had a weight gain of

more than 15 kgs , 15 % had a weight gain of less than 5 kgs . Data on III Trimester weight was not available for 12 women who had delivered.

Figure 8 -Mode of delivery:

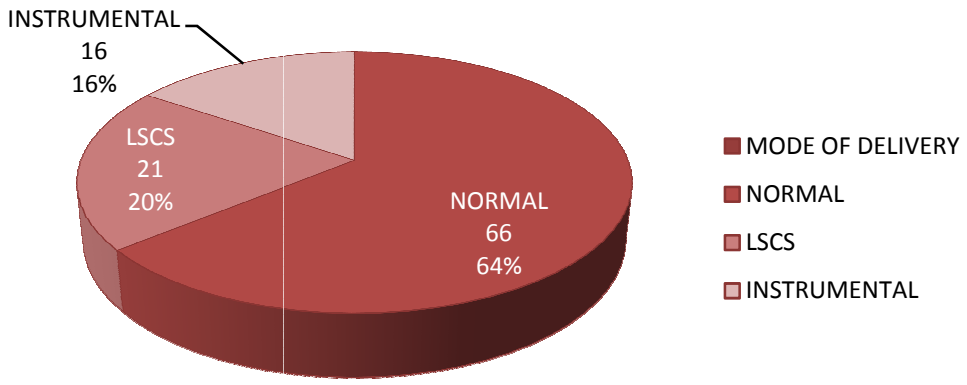


Figure 8 shows the mode of delivery for the women enrolled in the study. Sixty six percent delivered normally, 16 % had an instrumental delivery and 20 % underwent LSCS.

Variable	Average value	Standard deviation
Age of the participants(years)	25.5	4.17
Gestational age at delivery(weeks)	38.3	1.52
Weight gain in pregnancy(kilograms)	10.7	5.41

Figure 9 : Gestational age at delivery

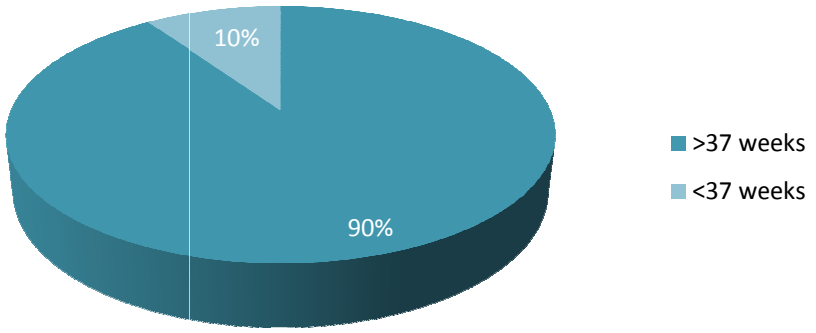


Figure 9 shows the gestational age at delivery. Ninty percent delivered at term >37 weeks. Only ten percent delivered preterm (<37 weeks).

Figure .10- Sex of the babies born:

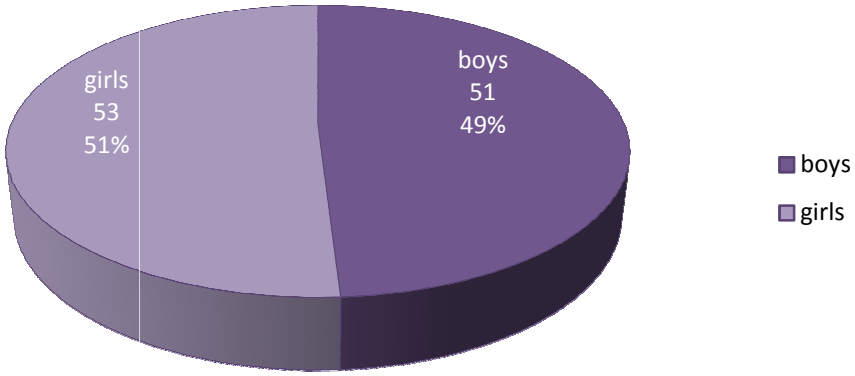


Figure 10 shows the sex distribution of the babies born to the study subjects . There was almost an equal distribution of boy and girl babies .

Figure .11-Birth weight distribution :

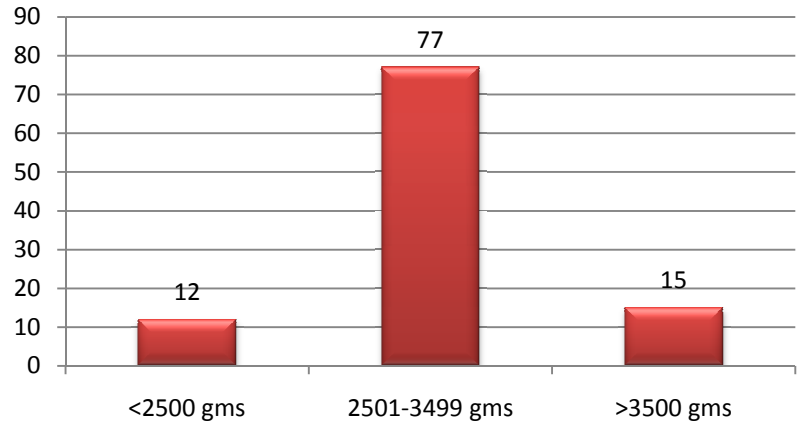


Figure 11 shows the categorisation of babies as per birth weight . Categories were Low birth weight <2500 grams ,normal weight between 2501-3500 grams, Large for gestational age (LGA) as >3500 grams. Seventy three percent (n=77) were in the normal weight group, 14 % (n=15) were in the LGA group and 11 % (n=12) were in the low birth weight group.

Table.1- Anthropometry of the babies born;

Parameter	Mean	Standard deviation
Birth grams	3027	555.48
Length(centimetres)	48.27	2.68
Ponderal index	2.65	0.393

Table .1 shows the average birth weight and birth length of the babies born, which was 3027 grams,the average length of the babies born was 48 cm

Figure .12 -Lipid Profile in I Trimester:

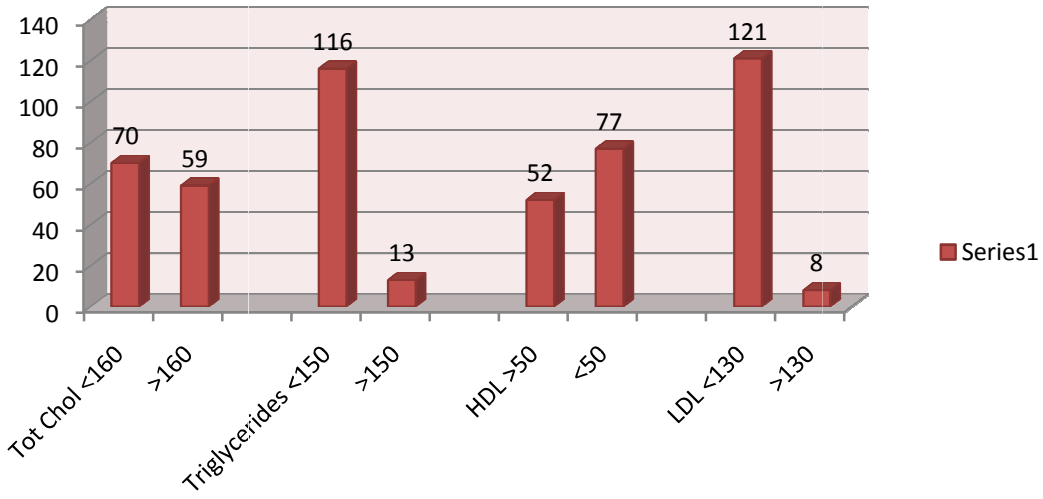


Figure 12 shows the pattern of lipid profile done in the first trimester. Fifty five percent (n=70) had I trimester cholesterol value < 160 mg /dl .Forty five percent (n=59) had a cholesterol value > 160 mg /dl which was considered as dyslipidemia. Eighty nine percent (n=116) had a I trimester Triglyceride < 150 mg /dl and ten percent had a triglyceride of > 150 mg /dl which was considered as dyslipidemia. Forty percent had normal I trimester HDL value >50 mg /dl and sixty had abnormally low HDL < 50 mg/dl, considered as dyslipidemia. With regard to LDL values, ninty three percent had normal LDL values < 130 mg/dl and seven percent had high I trimester LDL values > 130 mg/dl considered as dyslipidemia.

Figure .13-Dyslipidemia in I Trimester:

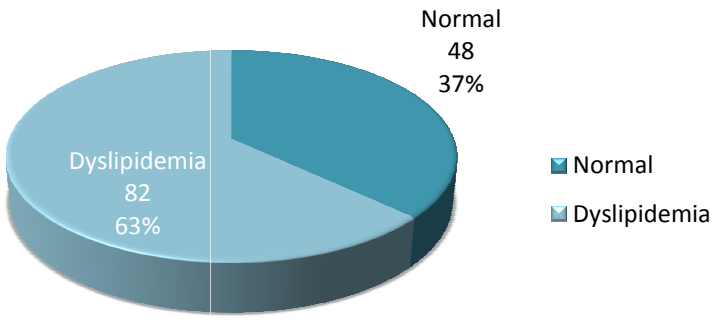


Figure 13 shows the dyslipidemia in I trimester. Sixty three percent (n=82) had dyslpidemia in the I trimester (cholesterol >160 mg/dl , triglycerides >150 mg/dl, HDL < 50 mg/dl and LDL > 130 mg/dl) and 37 % had normal lipid profile values.

Figure 14.-Gestational Diabetes Mellitus:

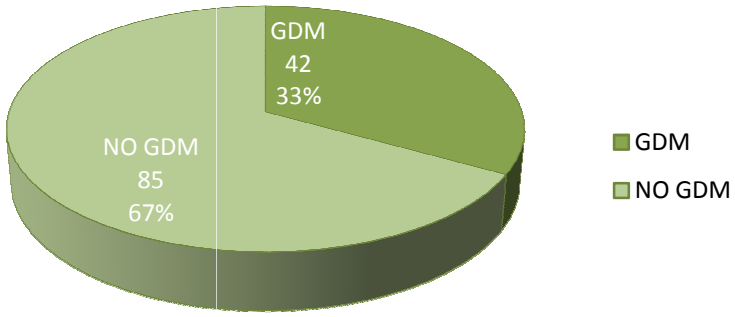


Figure 14 shows the incidence of Gestational diabetes mellitus in the population under study..Thirty three percent (n=42) of the women were diagnosed to have GDM and the remaining had normal glycemic profile.

Figure .15-Gestational hypertension:

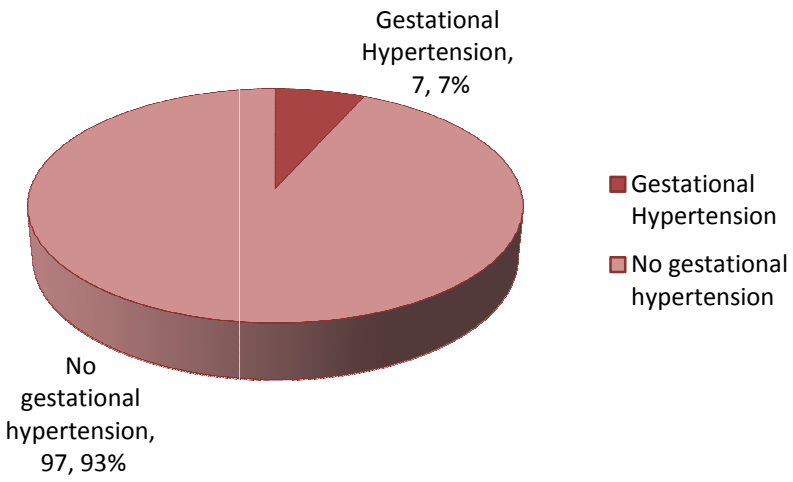
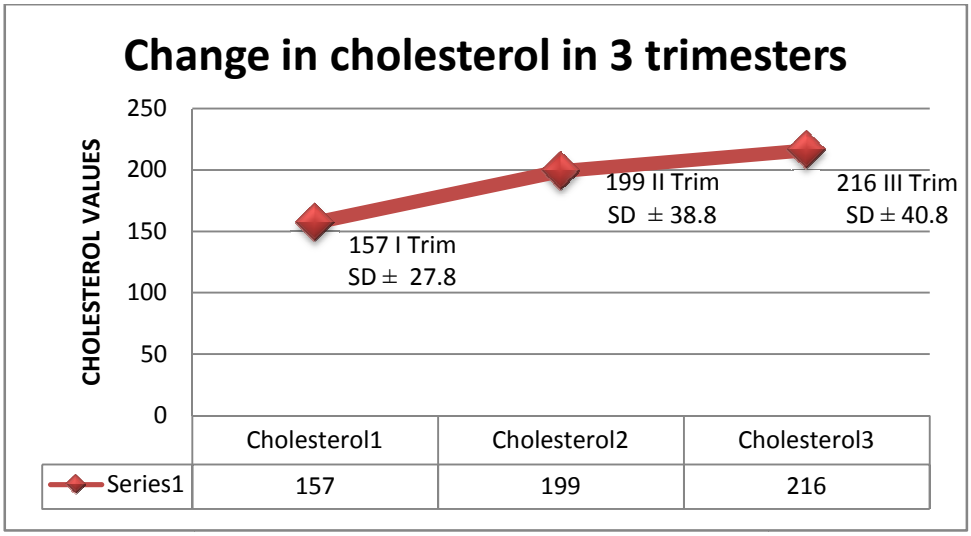


Figure 15 shows the incidence of Gestational hypertension in the women enrolled.Ninty three percent had normal blood pressure and only 7 % were diagnosed to have gestational hypertension.

Figure 16. Changes in cholesterol value over the three trimesters:

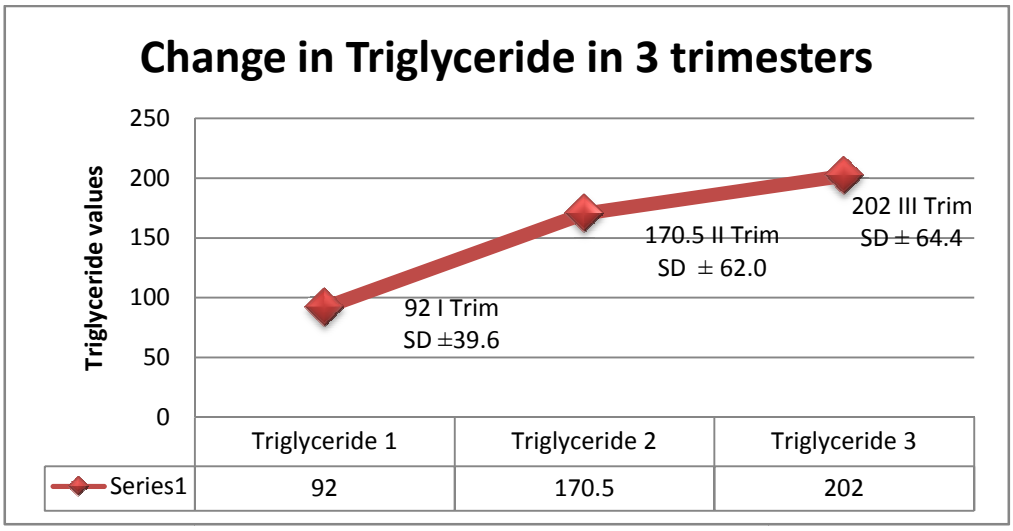


Percentage change _____30.5 %_____8%_____

Figure 16 shows the pattern of increase in cholesterol from the I trimester , through II and III trimester. The average value of cholesterol in I trimester

was 157 mg/dl, II trimester was 199 mg/dl, III trimester was 216 mg/dl. These values were calculated for the 76 women only , who had given all 3 lipid profiles.

Figure 17. **Changes in triglyceride value over the three trimesters**:

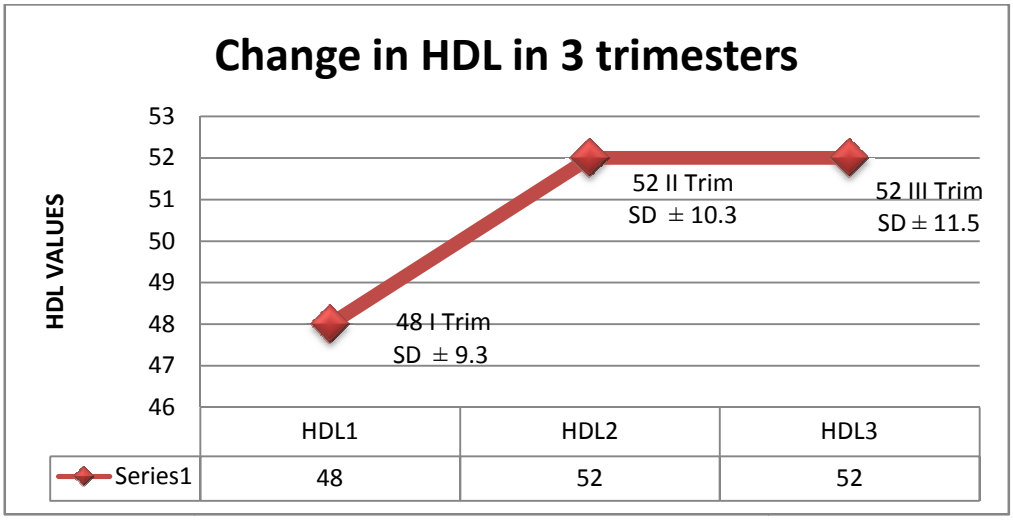


Percentage change_____84 %_____18%_____

Figure 17 shows the increase in the triglyceride levels over the three trimesters.The average triglyceride in I trimester was 92 mg/dl, II trimester was 170 mg/dl and III trimester was 202 mg/dl.

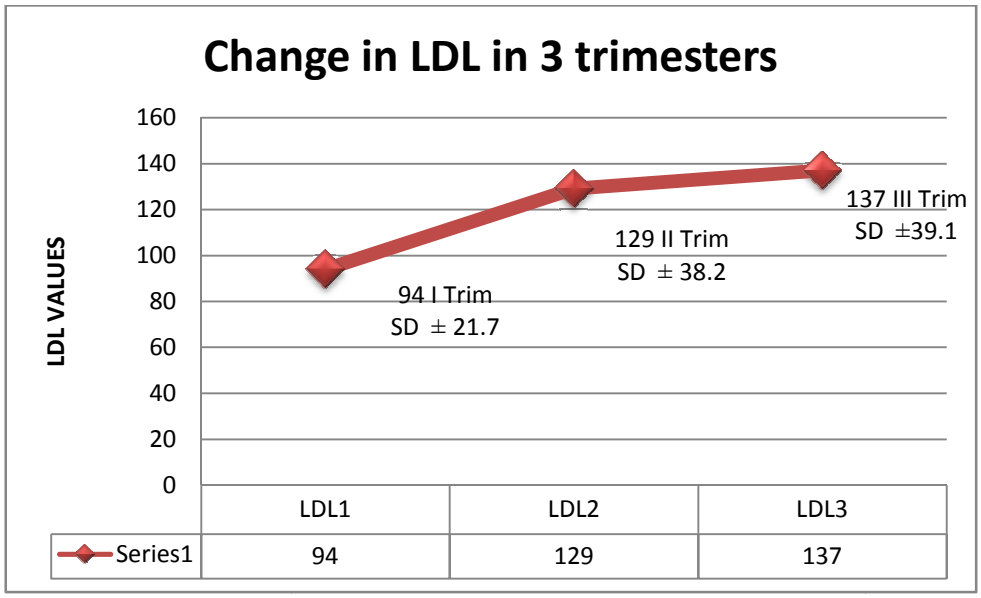
Figure 18- Changes in HDL value over the three trimesters:

Figure 18 shows the average values of HDL as measured in the three trimesters of pregnancy.The average HDL in I trimester was 48 mg /dl, II trimester was 52 mg/dl and III trimester was 52 mg /dl.



Percentage increase _____8 %_____0%_____

. **Figure 19. Changes in LDL value over the three trimesters**:



Percentage increase_____37 %_____6%_____

Figure 19 depicts the trend in the average LDL values over the three trimesters.The average LDL in I trimester was 94 mg/dl, II trimester was 129mg/dl and III trimester was 137 mg/dl.

Figure 20 Percentage of change between I & III trimesters :

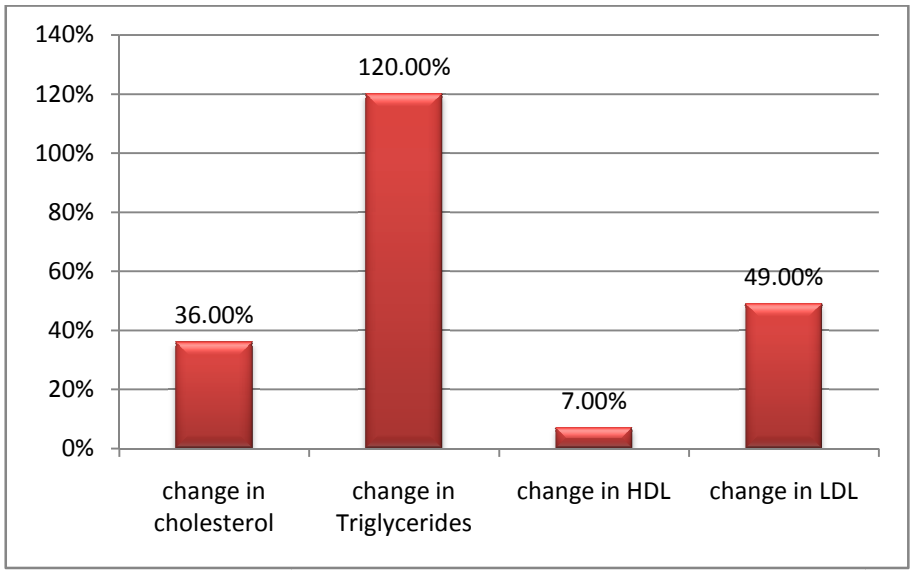


Figure 20 depicts the percentage increase in lipid values from I to the III trimester. Cholesterol increased by 36 %, triglycerides increased by 120 %, HDL by 7 % and LDL by 49 %.

Table 2.Cholesterol profile in 3 trimesters

	Mean	SD	Minimum	Maximum
Cholesterol I(mg/dl)	158	27.8	77	248
Cholesterol II(mg/dl)	203	38.8	120	383
Cholesterol III (mg/dl)	218	40.8	138	345

Table 2 shows the average cholesterol values in each trimester .In I trimester, the mean was 158 mg/dl with a SD of 27.8, in II trimester the mean was 203 with a SD of 38.8 and in III trimester ,the mean was 218 with a SD of 40.8.($p<0.00$)

Table 3.TRIGLYCERIDES:

	Mean	SD	Minimum	Maximum
Triglycerides I(mg/dl)	100	39.6	40	335
Triglycerides II(mg/dl)	178	62.0	87	620
Triglycerides III(mg/dl)	212	64.4	113	558

Table 3 shows the average triglyceride values in each trimester .In I trimester, the mean was 100 mg/dl with a SD of 39.6, in II trimester the mean was 178 with a SD of 62.0 and in III trimester ,the mean was 212 with a SD of 64.4.($p<0.01$)

.Table 4**.HDL**

	Mean	SD	Minimum	Maximum
HDL I (mg/dl)	48	9.3	33	77
HDL II (mg/dl)	54	10.3	32	77
HDL III (mg/dl)	54	11.5	34	85

Table 4 shows the average HDL values in each trimester .In I trimester, the mean was 48 mg/dl with a SD of 9.3, in II trimester the mean was 54mg/dl with a SD of 10.3 and in III trimester ,the mean was 54 mg/dl with a SD of 11.5.($p<0.01$)

Table 5.**LDL**

	Mean	SD	Minimum	Maximum
LDL I (mg/dl)	94	21.7	41	168
LDL II (mg/dl)	130	38.2	11	272
LDL III (mg/dl)	142	39.1	69	255

Table 5 shows the average LDL values in each trimester .In I trimester, the mean was 94 mg/dl with a SD of 21.7, in II trimester the mean was 130mg/dl with a SD of 38.2 and in III trimester ,the mean was 142 mg/dl with a SD of 39.1.($p<0.01$)

Variation between the three Trimesters:

Table 6 : Mean change between Cholesterol in I, II and III trimesters done by the **paired 't' test**.

CHOLESTEROL		Mean	Standard Deviation	Significance
Difference between I and II	I	158	27.8	P 0.000
	II	203	38.8	
Difference between II and III	II	203	38.8	P 0.001
	III	218	40.8	
Difference between I and III	I	158	27.8	P 0.000
	III	218	40.8	

Table 6 shows the mean change in the cholesterol values between the I & II trimester, between II & III trimester and between the I & III trimester with p value of <0.01 showing significant change between the trimesters.

Table 7: Mean change between Triglyceride in I, II and III trimesters

TGL		Mean	Standard Deviation	Significance
Difference between	I	100	39.6	0.000

I and II	II	178	62.0	
Difference between II and III	II	178	62.0	0.000
	III	212	64.4	
Difference between I and III	I	100	39.6	0.000
	III	212	64.4	

Table 7 shows the change in the triglyceride values between the I & II trimester, between II & III trimester and between the I & III trimester with p value of <0.01 showing significant change between the trimesters.

Table 8 : Mean change in HDL and LDL across I, II and III trimesters :

HDL		**Mean**	**Standard Deviation**	**Significance**
Difference between I and II	I	48	9.3	0.000
	II	54	10.3	
Difference between II and III	II	54	10.3	0.168
	III	54	11.5	
Difference between I and III	I	48	9.3	0.001
	III	54	11.5	
LDL		Mean	Standard Deviation	Significance
Difference between I and II	I	94	21.7	0.000
	II	130	38.2	
Difference between II and III	II	130	38.2	0.004
	III	142	39.1	
Difference between I and III	I	94	21.7	0.000
	III	142	39.1	

Table 8 shows the change in the HDL values between the I & II trimester, between II & III trimester and between the I & III trimester with p value of <0.01 showing significant change between the I & II , I & III trimesters.Between II & III trimesters HDL , p value was 0.168 , which was not significant.

Table 8 also shows the change in the LDL values between the I & II trimester, between II & III trimester and between the I & III trimester with p value of <0.01 showing significant change between the trimesters.

Table 9.**Correlation between birthweight and cholesterol in I , II & III trimesters**

. **Bi-Variate analysis** was done with Pearson correlation coefficients.

Birth grams		**Chol 1**	**Chol 2**	**Chol 3**
Pearson	Correlation co-efficient(r)	-0.126	-0.382	-0.202
	Significance	0.303	0.001	0.096

Table 9 shows the correlation between the birth weight and cholesterol values in all 3 trimesters. There was an inverse correlation between birth weight and cholesterol values in II trimester.

Table 10 Correlation between birthweight and Triglyceride in I , II & III trimesters using Bi-Variate analysis

Birth grams		**TGL 1**	**TGL 2**	**TGL 3**
Pearson	Correlation co-efficient(r)	0.080	-0.080	0.014
	Significance	0.512	0.509	0.909

Table 10 shows the correlation between the birthweight and triglyceride values in all 3 trimesters.There was a no correlation between birthweight and triglyceride values in all three trimesters.

Table 11 Correlation between birthweight and HDL in I , II & III trimesters using Bi-Variate analysis:

Birth grams		HDL 1	HDL 2	HDL 3
Pearson	Correlation co-efficient(r)	-0.218	-0.288	-0.217
	Significance	0.070	0.016	0.071

Table 11 shows the correlation between the birthweight and HDL values in all 3 trimesters.There was a inverse correlation between birthweight and HDL values in II trimester.

Table 12 Correlation between birthweight and LDL in I , II & III trimesters using Bi-Variate analysis

Birth grams		LDL 1	LDL 2	LDL 3
Pearson	Correlation co-efficient(r)	-0.068	-0.339	-0.084
	Significance	0.578	0.004	0.489

Table 12 shows the correlation between the birthweight and LDL values in all 3 trimesters.There was a inverse correlation between birthweight and LDL values in II trimester.

ABNORMAL LIPIDS AND GESTATIONAL DIABETES MELLITUS:

Table 13.GDM & Triglycerides of I trimester

		TRIGLYCERIDES			Significance(Fisher's exact test)
		Normal <150	High >150	TOTAL	
GDM	GDM	25	4	29	0.417
	NO GDM	44	3	47	
	TOTAL	69	7	76	

This shows the proportion of women who had high triglycerides in I trimester and later on developed GDM . Among those who had high triglycerides ,there was no significant statistical difference between those who developed GDM and those who did not.

Table 14 .GDM & Cholesterol of I Trimester:

		CHOLESTEROL			Significance(Fisher's exact test)
		Normal <160	High >160	TOTAL	0.059
GDM	GDM	11	18	29	
	NO GDM	29	18	47	
	TOTAL	40	36	76	

This shows the proportion of women who had high cholesterol in I trimester and later on developed GDM . Among those who had high cholesterol in I trimester ,there was no significant statistical difference between those who developed GDM and those who did not.

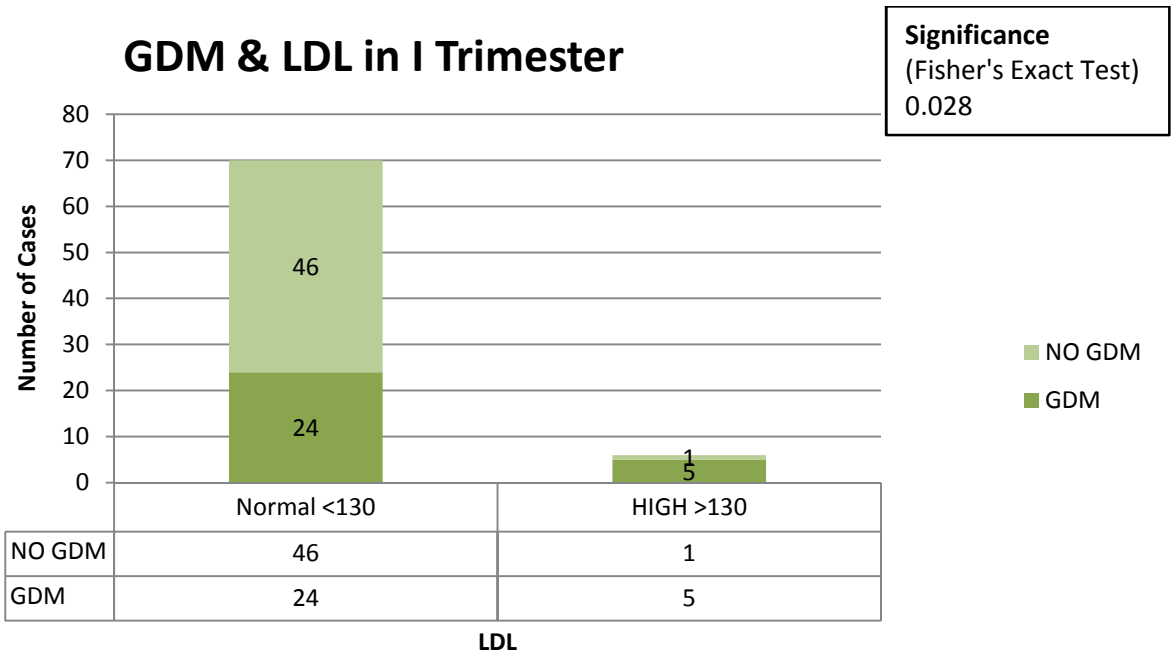
Table 15.GDM & HDL in I Trimester:

		HDL			Significance(Fisher's exact test)
		Normal >50	LOW <50	TOTAL	0.813
GDM	GDM	12	17	29	
	NO GDM	18	29	47	
	TOTAL	30	46	76	

This shows the proportion of women who had low HDL in I trimester and later on developed GDM . Among those who had low HDL (N=46) in I trimester ,there was no significant statistical difference between those who developed GDM and those who did not.

Table 16 GDM & LDL in I Trimester:

		LDL			Significance(Fisher's exact test)
		Normal <130	HIGH >130	TOTAL	0.028
GDM	GDM	24	5	29	
	NO GDM	46	1	47	
	TOTAL	70	6	76	



This shows the proportion of women who had high LDL in I trimester and later on developed GDM .There was significant statistical difference between those who developed GDM and those who did not, with I trimester LDL.

Table 17 .GDM & MODE OF DELIVERY:

		MODE OF DELIVERY			Significance(Fisher's exact test)
		Normal	LSCS	TOTAL	
GDM	GDM	**20**	**5**	**25**	**0.769**
	NO GDM	**32**	**11**	**43**	
	TOTAL	**52**	**16**	**68**	

This shows the proportion of women who had GDM and those who underwent LSCS. Among those who underwent LSCS ,there was no significant statistical difference between those who developed GDM and those who did not.

Table 18 WEIGHT OF THE BABY & MODE OF DELIVERY:

		MODE OF DELIVERY			Significance(Fisher's exact test)
		Normal	LSCS	TOTAL	
LGA	<3500	**42**	**15**	**57**	**0.437**
	>3500	**10**	**1**	**11**	
	TOTAL	**52**	**16**	**68**	

This shows the proportion of babies who weighed more than 3500 gms at birth and were delivered by LSCS .There was no statistical significance between mode of delivery and birth weight > 3500 gms.

Table 19 .WEIGHT OF THE BABY & HDL IN I TRIMESTER:

		HDL			Significance(Fisher's exact test)
		Normal >50	LOW <50	TOTAL	
LGA	<3500	23	36	59	1.000
	>3500	4	7	11	
	TOTAL	27	43	70	

This shows the proportion of women with abnormal HDL in I trimester and had babies weighing more than 3500 grams. There was no significant statistical association noted between abnormal HDL and birth weight of the baby.

Table 20.WEIGHT OF THE BABY & LDL IN I TRIMESTER:

		LDL			Significance(Fisher's exact test)
		Normal <130	HIGH>130	TOTAL	
LGA	<3500	53	6	59	0.580
	>3500	11	0	11	
	TOTAL	64	6	70	

There was no significant statistical association between abnormal LDL in I trimester and birth weight of the baby.

Table 21 WEIGHT OF THE BABY & CHOLESTEROL IN I TRIMESTER:

		CHOLESTEROL			Significance(Fisher's exact test)
		Normal <160	HIGH>160	TOTAL	
LGA	<3500	32	27	59	0.744
	>3500	7	4	11	
	TOTAL	39	31	70	

This shows the proportion of women who had high cholesterol in I trimester and had babies weighing more than 3500 grams. Among those who had high cholesterol in I

trimester ,there was no significant statistical difference between those who gave birth to LGA babies and those who did not.

Table 22 WEIGHT OF THE BABY & TRIGLYCERIDES IN I TRIMESTER:

		TRIGLYCERIDES			Significance(Fisher's exact test)
		Normal <150	HIGH>150	TOTAL	
LGA	<3500	55	4	59	0.482
	>3500	9	2	11	
	TOTAL	64	6	70	

This shows the proportion of women who had high triglycerides in I trimester and had babies weighing more than 3500 grams. Among those who had abnormal triglycerides in I trimester ,there was no significant statistical difference between those who gave birth to LGA babies and those who did not.

Table 23 .LOW BIRTH WEIGHT & HDL IN I TRIMESTER:

		HDL			Significance(Fisher's exact test)
		Normal >50	LOW<50	TOTAL	
LOW BIRTH WEIGHT	<2500	3	4	7	1.000
	>2500	24	39	63	
	TOTAL	27	43	70	

This shows the proportion of women who had abnormal HDL in I trimester and had babies weighing less than 2500 grams. Among those who had abnormal HDL in I trimester ,there was no significant statistical difference between those who gave birth to babies weighing less than 2500 grams and those who did not.

Table 24.LOW BIRTH WEIGHT & LDL IN I TRIMESTER:

		LDL			Significance(Fisher's exact test)
		Normal <130	HIGH>130	TOTAL	
LOW BIRTH WEIGHT	<2500	5	2	7	0.107
	>2500	59	4	63	
	TOTAL	64	6	70	

This shows the proportion of women who had abnormal LDL in I trimester and had babies weighing less than 2500 grams. Among those who had high LDL in I trimester ,there was no significant statistical difference between those who gave birth to babies weighing less than 2500 grams and those who did not.

Table 25: LOW BIRTH WEIGHT & CHOLESTEROL IN I TRIMESTER:

		CHOLESTEROL			Significance(Fisher's exact test)
		Normal <160	HIGH>160	TOTAL	0.692
LOW BIRTH WEIGHT	<2500	3	4	7	
	>2500	36	27	63	
	TOTAL	39	31	70	

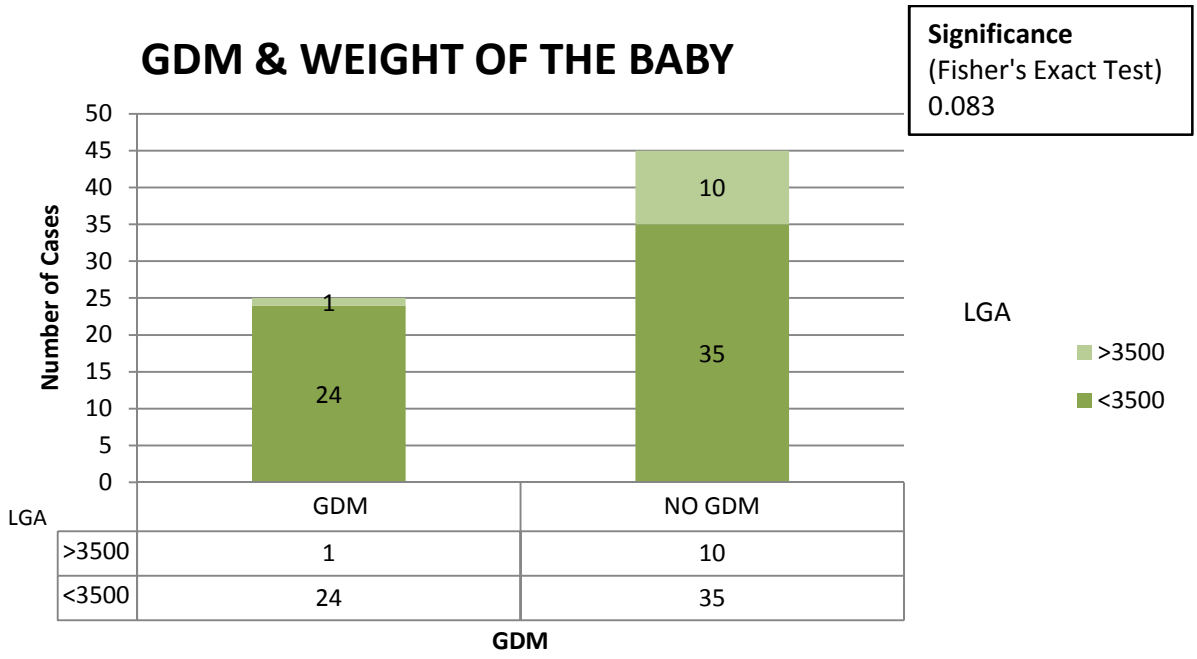
This shows the proportion of women who had abnormal cholesterol in I trimester and had babies weighing less than 2500 grams. Among those who had high cholesterol in I trimester ,there was no significant statistical difference between those who gave birth to babies weighing less than 2500 grams and those who did not.

Table 26 .LOW BIRTH WEIGHT & TRIGLYCERIDES IN I TRIMESTER:

		TRIGLYCERIDES			Significance(Fisher's exact test)
		Normal <150	HIGH>150	TOTAL	0.482
LOW BIRTH WEIGHT	<2500	6	1	7	
	>2500	58	5	63	
	TOTAL	64	6	70	

This shows the proportion of women who had abnormal triglycerides in I trimester and had babies weighing less than 2500 grams. Among those who had high triglyceride in I trimester ,there was no significant statistical difference between those who gave birth to babies weighing less than 2500 grams and those who did not.

Table 27.GDM & WEIGHT OF THE BABY:



This shows the proportion of women who had GDM and had babies weighing more than 3500 grams. Among those who delivered babies weighing more than 3500 grams ,there was no significant statistical difference between those who had GDM and those who did not.

		GDM			Significance(Fisher's exact test)
		GDM	NO GDM	TOTAL	
LGA	<3500	24	35	59	0.083
	>3500	1	10	11	
	TOTAL	25	45	70	

Table 28 .WEIGHT GAIN & WEIGHT OF THE BABY (LGA):

		WEIGHT GAIN			Significance(Fisher's exact test)
		<15 KG	>15 KG	TOTAL	
LGA	<3500	48	8	56	0.171
	>3500	6	3	9	
	TOTAL	54	11	65	

This shows the proportion of women who gained more than 15 kilograms in pregnancy and had babies weighing more than 3500 grams. Among those who gained more than 15 kilograms ,there was no significant statistical difference between those who gave birth to babies weighing more than 3500 grams and those who did not.

Table 29 WEIGHT GAIN & ABNORMAL LIPIDS IN I TRIMESTER(LDL):

		WEIGHT GAIN			Significance(Fisher's exact test)
		<15 KG	>15 KG	TOTAL	
LDL	<130 NORMAL	48	11	56	0.579
	>130 HIGH	6	0	9	
	TOTAL	54	11	65	

This shows the proportion of women who gained more than 15 kilograms in pregnancy and had abnormal LDL in I trimester . Among those who gained more than 15 kilograms ,there was no significant statistical difference between those who had high LDL in I trimester and those who did not.

Table 30.WEIGHT GAIN & CHOLESTEROL IN I TRIMESTER :

		WEIGHT GAIN			Significance(Fisher's exact test)
		<15 KG	>15 KG	TOTAL	
CHOLESTEROL	<160 NORMAL	30	5	35	0.742
	>160 HIGH	24	6	30	
	TOTAL	54	11	65	

This shows the proportion of women who gained more than 15 kilograms in pregnancy and had abnormal cholesterol in I trimester . Among those who gained more than 15 kilograms ,there was no significant statistical difference between those who had high cholesterol in I trimester and those who did not.

Table 31.WEIGHT GAIN & TRIGLYCERIDES IN I TRIMESTER :

		WEIGHT GAIN			Significance(Fisher's exact test)
		<15 KG	>15 KG	TOTAL	1.000
TRIGLYCERIDES	<150 NORMAL	50	10	60	
	>150 HIGH	4	1	5	
	TOTAL	54	11	65	

This shows the proportion of women who gained more than 15 kilograms in pregnancy and had abnormal triglycerides in I trimester . Among those who gained more than 15 kilograms ,there was no significant statistical difference between those who had high triglycerides in I trimester and those who did not.

Table 32 WEIGHT GAIN & HDL IN I TRIMESTER:

		WEIGHT GAIN			Significance(Fisher's exact test)
		<15 KG	>15 KG	TOTAL	0.743
HDL	>50 NORMAL	21	5	26	
	<50 LOW	33	6	39	
	TOTAL	54	11	65	

This shows the proportion of women who gained more than 15 kilograms in pregnancy and had abnormal HDL in I trimester . Among those who gained more than 15 kilograms ,there was no significant statistical difference between those who had low HDL in I trimester and those who did not.

Figure 33 .WEIGHT GAIN & LOW BIRTH WEIGHT :

		WEIGHT GAIN			Significance(Fisher's exact test)
		<5 KG	>5 KG	TOTAL	1.000
LOW BIRTH WEIGHT	< 2500	1	11	12	
	>2500	5	49	54	
	TOTAL	6	60	66	

This shows the proportion of women who gained less than 5 kilograms in pregnancy and delivered babies weighing less than 2500 grams . Among those who gained less than 5 kilograms ,there was no significant statistical difference between those who had babies weighing less than 2500 grams and those who did not.

Table 34 Factors influencing weight of the baby

Logistic regression analysis was done to see if weight gain of the mother, cholesterol, HDL, LDL and triglycerides in III trimester had an influence on the birth weight.

Variables	Beta coefficient	significance	95 % confidence interval	
Weight gain	25.17	0.01	5.52	44.83
cholesterol	-1.92	0.65	-10.29	6.49
triglycerides	0.68	0.68	-2.6	3.95
HDL	-6.30	0.31	-18.6	6.08
LDL	2.05	0.68	-7.86	11.97

Beta coefficient refers to the amount of change in birth weight for an unit change in the factors affecting birth weight. Only weight gain of the mother showed a significant influence (p 0.01) on the birth weight of the baby.For every 1 kilogram increase in weight of the mother , there will be 25 grams increase in the birth weight of the baby.

Table 35.Correlation between percentage change in lipids between I & III trimester and developing GDM

Lipid profiles	GDM						p-value
	No GDM			GDM			
	25th percentile	Median	75th percentile	25th percentile	Median	75th percentile	
Cholesterol	20.41	33.96	50.78	21.35	37.95	59.33	0.65
Trigycerides	65.63	114.63	166.42	60.93	146.36	196.7	0.31
HDL	2.22	11.43	27.27	-10.53	4	14.29	0.03
LDL	18.1	45.45	76	34.04	55.67	84.72	0.16

The above table shows no statistically significant correlation between the percentage change in lipid values (Cholesterol/Triglycerides/LDL) between I & III trimester and the risk of developing GDM. There is significant correlation between percentage change in HDL and developing GDM.

DISCUSSION

BASELINE DEMOGRAPHY

Among the hundred and thirty women who were recruited ,lipid profile was available for all three trimesters , only in seventy six women. The most probable reason could be , that these women went to their mother's place after the first trimester for further antenatal care or they had adverse pregnancy outcomes like abortion, preterm labour etc for which they did not come to CMCH for medical treatment.The mean age of the women recruited was 25.5 years. The majority were in the reproductive age group of 18-30 years. The majority (75 %)of the patients enrolled were in middle socioeconomic strata and almost equal distribution in the high and low strata.

At baseline, 31 % of the women were in the obese group, 17 % in the overweight group and only 34 % were in the normal BMI category. According to Indian statistics, 5 % of our population are obese. According to the National Family Health Survey (NFHS), the percentage of ever married women aged 15-49 years who are overweight or obese increased from 11% in NFHS-2 to 15% in NFHS-3. Under nutrition is more prevalent in rural areas, whereas overweight and obesity are more than three times higher in urban areas. In south India the percentage of women who are overweight or obese is highest in Kerala (34%), followed by Tamil Nadu (24.4%), Andhra Pradesh (22.7%) and Karnataka (17.3%)(82).Overweight and obesity have been associated with development of diabetes, hypertension and cardiovascular events.

In pregnancy , more than one third of women were found to be obese in the U.S. Obesity leads to pregnancy related complications like gestational diabetes mellitus, gestational hypertension, pre eclampsia, higher rates of LSCS and increased post partum retention of weight. In the fetus,maternal obesity can lead on to increased

prematurity, stillbirths, congenital anomalies, macrosomia, birth injuries and childhood obesity. They can have intra operative complications, anaesthetic complications, deep vein thrombosis and delay in initiation of breast feeding(85). The characteristic pattern in lipid profile among obese people, consists of elevated serum low-density lipoprotein cholesterol (LDL-C) and triglycerides and lowered high-density lipoprotein cholesterol levels(83,84)

PREGNANCY RELATED OUTCOMES :

Weight gain in pregnancy: The average weight gain in pregnancy found in our study was about 10 kilograms which is less than the normal range of weight gain (11-16 kilograms for BMI between 18.5-24.9) recommended. About 57 % of the participants had a weight gain between 5-15 kilograms. From previous studies, pre conceptional BMI of the woman , level of physical activity were the strong predictors of weight gain in pregnancy , more than genetic factors, age, parity and nutrition levels(86).Excessive weight gain in pregnancy has been quoted as the strongest determinant of maternal post partum weight retention, associated with long term weight gain , body adiposity and obesity – independent of age, predictor of high birthweight , macrosomia and overweight in infancy(87–91).

Mode of delivery : The majority (66 %) of the women delivered vaginally and LSCS rate was 20 % which corresponds to our institution's LSCS rate of 22-25 %.

Timing of delivery : Most of the women delivered at term , only 6 % had a pre term delivery. The average gestational age at delivery was 38 weeks.

Sex of the babies born : There was an equal distribution of boys: girls born .The National sex ratio, girl : boy is 806 : 1000 , attributed to female infanticide and feticide(92).

Birth weight: Seventy three percent of the babies born were within the normal range of 2500 grams to 3500 grams. Fourteen percent (n=15) were over 3500 grams and eleven percent were in the low birth weight group < 2500 grams. The birth weight of average Indian babies has been between 2500 grams to 2700 grams(93).

BASELINE LIPIDS IN PREGNANCY:

Dyslipidemia: Dyslipidemia are disorders of lipoprotein metabolism, including lipoprotein overproduction and deficiency which is associated with obesity regardless of ethnic group. They may marked as one or more of the following: elevated total cholesterol, Low-density Lipoprotein Cholesterol (LDL), and triglyceride levels or as decreased High-Density Lipoprotein Cholesterol (HDL) level with promotion of insulin resistance causing metabolic syndrome in obesity(83). With the above criteria,63 % (n=82) of the women recruited were found to be dyslipidemic. Low HDL , defined as HDL < 50 mg /dl contributed to the majority in the dyslipidemia group. Dyslipidemia in reproductive age group is usually associated with polycystic ovarian syndrome. Lifestyle modification with diet to control dyslipidemia , thereby reducing future cardiovascular disease risk has been well studied in men and women in non reproductive age group.

In the Framingham study , the ratio of Total cholesterol : HDL was considered as excellent predictor of CHD risk with a hazard ratio of 1.21 for a 1.0 increment in ratio(94).In the Helsinki Heart study, LDL : HDL ratio , proved to be a better predictor of CHD , specially with associated hypertriglyceridemia. However , low HDL in this age group, may be an important predictor of CHD later in life. Lifestyle modification , with exercise, diet changes, cessation of smoking etc may alter the long term risks of development of CHD, if started early in life.

Gestational Diabetes Mellitus and Gestational hypertension:

There was an incidence of 33 % of GDM seen in this study. In India, gestational diabetes mellitus was found to be complicating 16.5 % of pregnancies in 2004 (95) and the trend has been steadily increasing. We have recorded an incidence of 15 % in our CMCH obstetrics department . With regard to lipid profile in pregnancy, baseline LDL , mainly atherogenic small, dense LDL III fractions, was high in pregnancies complicated by GDM and showed a higher increase over the three trimesters compared to normal pregnancy(96).

Gestational hypertension was seen in six percent of the women recruited. Worldwide the incidence of gestational hypertension has been 2-3 % and CMCH statistics show an incidence of 10-11 % .

CHANGES IN LIPID PROFILE OVER THE THREE TRIMESTERS OF PREGNANCY

Cholesterol: Total cholesterol ,showed an increasing trend from I to III trimester of pregnancy. The average percentage in increase was 36 % . This was little less than what has been reported in literature earlier, which was 43-53 % rise in cholesterol over the three trimesters of pregnancy(71,72). Also , there was significant change in the mean cholesterol levels between I & II, II & III and I & III trimesters of pregnancy.

Triglyceride : Triglycerides also showed an increasing trend as pregnancy advanced. The percentage increase , seen in this study was 120 %, compared to 150-230 % rise ,reported earlier(71,72). Also , there was significant change in the mean triglyceride levels between I & II, II & III and I & III trimesters of pregnancy.

HDL ;. HDL showed an increase of 7 % from I to III trimester . 0-25 % increase has been reported earlier, in other studies. There was significant change in the mean HDL levels between I & II and I & III trimesters of pregnancy. But no change between II & III trimester.

LDL : LDL also showed an increase in average value from I to III trimester of 49 % which was similar to 36-40 % increase ,reported in literature earlier. There was significant change in the mean LDL levels between I & II, II & III and I & III trimesters of pregnancy.

This pattern of increase in total cholesterol, triglycerides, HDL and LDL throughout pregnancy is due to the relative insulin resistance that develops during the later half of pregnancy by the increasing placental hormones. There is a net breakdown of maternal fat deposits, leading to the increase in circulating lipids mainly triglycerides , which is essential for the growing fetus.

SUMMARY :

In answer to the first objective of the study to assess the longitudinal variation in lipids between the three trimesters, there was a significant increase in the Total cholesterol, triglyceride, LDL and HDL cholesterol between the three trimesters of pregnancy . Only the change between the HDL values in II & III trimester , was not statistically significant as there was no observable difference.

RELATION BETWEEN BIRTH WEIGHT OF THE BABY AND MATERNAL LIPID LEVELS.

Birth weight of the baby is strongly determined by the neonatal fat mass. As mentioned in earlier studies, maternal triglyceride , mainly in the II trimester significantly correlated with the birth of LGA baby(48). In well controlled GDM pregnancies, maternal lipids are the strong predictors of fetal lipids and fetal growth.Maternal FFA&TG measured close to term predicted LGA birthweight independent of maternal BMI(3). Among women without GDM, maternal adiposity & leptin levels were the strongest metabolic determinants of LGA baby than glucose intolerance & lipid levels(68). Failure of the normal rise in LDL by 60 % in III Trimester is found to be associated with IUGR(23).

In our study we did not find any significant positive association between maternal lipid profile (in each trimester) and the birth weight of the baby. Abnormal lipids in I trimester in the mother did not have any effect on the weight of the baby born. There was a negative correlation between weight of the baby and II trimester cholesterol, HDL and LDL..

SUMMARY

In answer to the second objective, no significant positive correlation was noticed between the lipid values in three trimesters and the birth weight. Negative correlation was observed between II trimester cholesterol, HDL, and LDL values with the birth weight of the baby which is a new observation.

BIRTHWEIGHT AND OTHER FACTORS :

Maternal weight gain , either a higher weight gain of more than 15 kilograms or a lower weight gain of less than 5 kilograms did not affect the birth weight of the baby in a significant manner. There was no significant association between weight gain of the mother in pregnancy and dyslipidemia in I trimester.

By logistic regression analysis, the linear weight gain of the mother ,in pregnancy was the only factor that had a significant effect on the baby's birth weight as compared to other factors like BMI, lipids and GDM. We found that , for every 1 kg increase in maternal weight , there was a 25 grams increase in the baby's birth weight. In a study by Waters et al, where the neonatal body composition was correlated with the weight gain in the mother according to IOM guidelines, they found that, increasing maternal weight gain during pregnancy significantly affects newborn fat mass, lean body mass, and percentage body fat. Increasing gestational weight gain disproportionately increased newborn fat mass relative to the observed increases in newborn lean body mass or percentage body fat . For normal BMI women, gestational weight gain had significant effects on newborn adiposity. Gestational weight gain was not a significant contributor to newborn adiposity for overweight or obese women(102).

LIPDS AND GESTATIONAL DIABETES MELLITUS /GESTATIONAL HYPERTENSION.

In previous studies, hypertriglyceridemic dyslipidemia before 20 weeks of GA was associated with risk of developing early but not early onset severe pre eclampsia(99). Endothelial dysfunction , the primary pathology in pre eclampsia, has been found to persist even after pregnancy, leading to an increased risk of CHD later in life. Dyslipidemia and hypertension are very closely associated with endothelial

dysfunction. Aberrations or an exaggeration of normal lipid profile changes , mainly an abnormally low HDL and a disproportionate increase in LDL has been observed in pregnancies complicated by pre eclampsia(100). In our study, number of women who developed gestational hypertension among those who delivered , in the study period was only 7. In view of the small number, no statistical analysis was performed to find the association between lipid profile and gestational hypertension.

With regard to gestational diabetes mellitus, previous literature states that triglyceride, measured between 9-12 weeks was most predictive of developing GDM in that pregnancy more for Asian women(3 fold increase) than western born women(58).In women with positive diabetic screening in pregnancy, Maternal triglyceride was significantly associated with birth weight, value >259 mg/dl was a significant predictor of LGA infants independent .of pre pregnancy BMI, maternal weight gain & fasting plasma glucose levels(48). Hypertriglyceridemia is the main lipid disorder in pregnant women with GDM, with a remarkable increase observed between second and third trimester(101).

In our study , 33 % of the women enrolled were diagnosed to have gestational diabetes mellitus which is almost double the incidence of GDM in our population which is 15 %. However there was no significant association between linear lipid profile changes in three trimesters and occurance of GDM . There was significant increase in lipid profile between each trimester, but the percentage increase did not affect the development of GDM. Dyslipidemia in I trimester also did not show any significant prediction of developing GDM later on in pregnancy.

SUMMARY :

Though the incidence of GDM was high 33 % , in this study, lipid profile in the women studied did not show statistically significant correlation with the risk of developing GDM and had no influence on the birth weight or mode of delivery.

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CONCLUSION

1. There was a significant increase observed, in the levels of total cholesterol,triglycerides, HDL and LDL between the three trimesters of pregnancy with triglycerides showing the maximum change.

2. Significant number of women , 63 % were dyslipidemic even in the I trimester which is a depictor of non pregnant values. The major contributor was low HDL <50 mg/dl, which is a potential risk factor for future cardiovascular diseases , hypertension and diabetes mellitus.

3.Lipid profile across the three trimesters did not significantly affect the birth weight of the baby.

4.There was no correlation between lipid profile changes and the risk of developing GDM in the women studied.

5.The incidence of GDM was almost double , 33 %, compared to what is observed in the population in South India.

6. The incidence of overweight (17 %) and obesity (31 %), at baseline was quite high compared to the reported prevalence of obesity in 24 % of women in reproductive age group in South India.

7.Weight gain in the mother ,was the only factor that showed significant correlation with birth weight .With every 1 kilogram weight gain , there was 25 grams increase in birth weight of the baby.

LIMITATIONS

1.Only 76/130 women enrolled in the first trimester , gave lipid profile in all three trimesters. Adequate follow up of all patients enrolled ,was deficient as the patients were distributed between 3 obstetric units which had OPD functioning on different days . These women were seen by different doctors at each visit as they are rotated between units each month. Hence adequate numbers were not available to prove statistical significance.

2. Only one hundred and four women had delivered before the time allotted for the completion of the study. This was due to late enrolment of patients.

3. Lipid profile , taken in post partum period , after 6 weeks would have given us a picture of how many women continued to have lipid profile values in the dyslipidemia range.

4.A detailed dietary history of all the patients in each trimester ,would have given extra information to correlate with lipid levels and birth weight of the baby.

5. Family history of dyslipidemia was not taken into account to identify women with genetic predisposition to dyslipidemia. Physical activity of the mother was not considered or quantified. That would have given more information on altering risk factors for dyslipidemia in the I trimester.

6.Normal lipid profile reference values for each trimester is not available . Cut off values for dyslipidemia is only available for non pregnant population.

FUTURE RESEARCH AVENUES

1. To obtain normal reference values for lipid profile in pregnancy for each trimester and to identify women who have abnormal values in each trimester of pregnancy, with a larger sample size.
2. To identify factors predisposing to dyslipidemia in reproductive age group and provide appropriate health education regarding modification of life style, diet and physical activity.
3. To provide long term follow up to the women who were dyslipidemic in I trimester and to identify early markers for development of diabetes, hypertension and cardiovascular diseases.

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APPENDIX 1

PROFORMA

LIPID PROFILE IN PREGNANCY

1.Name :

2.Age :

3.Hospital number :

4.Address :

5.Phone number :

6.SES : Low / Middle / High

7.Parity : G _ P_ L _

8.Diet : Veg / Non veg

9.Height : _____ cms

10.Weight

Prepregnancy : _____ Kg

I Trimester : _____ Kg

II Trimester : _____ Kg

III Trimester : _____ Kg

11.Blood Pressure

I Trimester : _____ mm Hg

II Trimester : _____ mm Hg

III Trimester : _____ mm Hg

12.Sugar Profile

AC :

GTT :_____ / _____ / _____

13.Mode of delivery :Normal / Instrumental / LSCS

14.GA at delivery : _____ Weeks

15.Sex of the baby : Boy / Girl

16.Birth weight : _____ Gms

17.Length of the baby : _____ Cms

18.Lipid Profile

	I TRIM	II TRIM	III TRIM
Total Cholesterol			
HDL			
LDL			
TGL			

APPENDIX 2

CONSENT FORM

Informed Consent form to participate in a research study :LIPID PROFILE IN PREGNANCY

Study Title:

Study Number:

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age:_____Please initial box

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. (ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. (iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. (iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ] v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

APPENDIX 3

ABBREVIATIONS

1.HDL –High Density Lipoprotein

2.LDL- Low density Lipoprotein

3.IUGR-Intra Uterine Growth Restriction

4.LGA-Large for gestational Age

5.LSCS-Lower Segment Caesarean Section

6.GDM –Gestational Diabetes Mellitus

7.TC- Total Cholesterol

8.TGL –Triglycerides

9.FA-Fatty acids

10.ACAT-Acyl Co A Transferase

11.LCAT-Lecithin Cholesterol acyl transferase.

12.CETP-Cholesterol Ester Transfer Protein

13.LCPUFA –Long Chain Polyunsaturated fatty acid

14.LPL-Lipoprotein Lipase

15.BMI-Body Mass Index

16.SHH-Sonic Hedge Hog signalling

17.CHD-Coronary Heart Disease

18.Kg-Kilograms

Data of all Women Recruited

s.no	name	cmch	age	ht	wt	wt_gain	sys_bp	dia_bp	sys_bp	dia_bp	ac	gtt_fast	gttt_1	gttt_2	mode_d	sex	weeks	days	birth_gr	length	ponder	ch_1	ch_2	ch_3	tg_1	tg_2	tg_3	hdl_1	hdl_2	hdl_3	ldl_1	ldl_2	ldl_3
1	ALMAS JABEEN	420602F	23	155	37	7	105	64	100	50	81	70	117	113	1	2	39	3	2,650	47	3	158	214	.	96	140	.	46	50	.	87	162	.
2	ANISA BEGUM	358311C	26	150	50	.	93	62	120	70	73	79	138	79	2	2	39	2	2,800	43	4	196	.	.	107	.	.	66	.	.	118	.	.
3	ANITHA	772814D	28	159	56	7	102	64	120	70	.	72	146	122	1	2	39	1	3,020	48	3	77	199	213	117	188	166	65	51	56	98	127	153
4	ANEES FATHIMA	399743F	23	153	59	13	110	70	120	70	85	78	82	132	1	1	40	1	2,980	49	3	140	214	211	79	180	220	45	67	60	83	11	128
5	ANEESHA NASREEN	794523D	21	160	39	17	118	77	120	80	94	77	105	98	1	1	39	4	2,880	48	3	120	.	241	40	.	137	45	.	65	64	.	168
6	ANITHA A	414588F	24	160	58	18	99	67	100	70	72	74	172	162	1	2	39	5	3,580	48	3	179	182	208	173	265	257	56	56	43	100	108	131
7	ARUNA	395029F	23	157	51	20	107	67	120	70	81	81	130	109	2	2	40	5	3,080	49	3	135	.	.	164	.	.	43	.	.	70	.	.
8	ASIYA	439967D	21	147	59	16	117	74	120	70	83	83	118	124	1	1	39	4	2,880	47	3	157	.	296	103	.	287	48	.	36	101	.	232
9	ASHA P	331096D	27	165	45	7	100	53	.	.	90	.	.	.	1	2	34	6	1	37	0	126	158	.	75	162	.	53	47	.	62	91	.
10	ATHIQA BANU	482868F	20	159	54	.	87	54	.	.	92	.	.	.	.	.	.	.	.	.	.	116	.	.	55	.	.	45	.	.	61	.	.
11	AYSHA KHANAM	418502F	20	158	63	13	113	69	160	110	.	67	86	116	1	1	38	1	2,580	47	2	138	199	180	82	125	176	43	61	49	86	132	114
12	BANUMATHI	610314C	33	173	68	9	103	65	120	70	95	.	.	.	1	1	38	4	3,070	50	2	150	184	188	151	193	243	37	48	45	94	120	126
13	BHARATHI	404012F	26	159	42	7	96	65	110	70	88	73	134	119	1	1	37	6	2,520	46	3	142	238	242	98	242	264	40	50	44	93	174	139
14	BHUVANA	939036D	25	150	43	9	105	69	110	80	72	.	.	.	1	2	39	4	2,390	47	2	144	198	186	102	163	186	57	73	59	77	100	112
15	BHUVANA	146870F	24	160	52	11	117	67	120	70	95	.	.	.	2	1	40	6	3,420	52	2	170	248	265	90	167	233	43	50	43	102	172	212
16	CAROLINE	993760C	35	160	67	.	120	80	.	.	96	.	.	.	.	.	.	.	.	.	.	147	.	.	45	.	.	47	.	.	94	.	.
17	CHANDRALEKHA	386534F	21	154	48	17	107	70	110	70	89	.	.	.	1	2	40	6	2,670	48	2	170	238	228	72	189	163	68	64	52	92	153	165
18	CHITRA C	578422D	25	154	60	14	109	70	120	80	89	81	121	113	2	1	39	1	2,920	48	3	136	186	164	82	140	152	57	65	60	70	103	92
19	CHELVI	383877F	23	165	64	16	98	68	110	60	92	77	116	109	1	2	40	2	3,420	50	3	163	.	238	92	.	260	62	.	49	87	.	134
20	DEEPA	069457F	22	155	53	.	106	67	120	70	81	108	120	105	1	1	37	4	3,150	49	3	247	269	.	183	218	.	56	56	.	166	190	.
21	DEEPA S	386259F	21	163	59	20	97	65	110	60	91	.	.	.	1	2	38	.	3,200	50	3	148	131	.	138	296	.	49	43	.	94	56	.
22	DEEPA	795190C	24	168	65	21	102	65	120	70	76	80	113	92	2	2	39	2	3,600	50	3	184	242	231	116	249	351	77	64	62	101	156	143
23	DHANALAKSHMI	391582F	23	162	74	11	106	66	110	70	78	74	123	110	2	1	39	.	3,100	48	3	151	219	155	82	181	160	49	69	64	77	110	81
24	DHANALAKSHMI G	473696F	26	152	63	.	95	66	.	.	95	.	.	.	.	.	.	.	.	.	.	142	147	.	88	133	.	36	42	.	91	93	.
25	DIVYA K	088528F	19	150	46	.	96	68	.	.	77	.	.	.	.	.	.	.	.	.	.	114	.	.	74	.	.	33	.	.	73	.	.

26	DILSHATH THABASUM	475359F	18	155	54	23	100	70	100	70	79	93	126	102	3	2	37	3	3,290	49	.	150	231	239	91	225	280	45	58	47	92	160	153
27	DIVYA	412156F	20	145	48	.	107	70	.	.	74	.	.	.	.	.	.	.	.	.	.	190	.	.	130	.	.	48	.	.	118	.	.
28	DIVYA	382952F	22	161	64	12	110	74	120	70	83	.	.	.	1	1	39	1	3,500	47	3	172	197	218	97	122	202	40	48	43	105	135	161
29	DIVYA	419691F	27	162	59	12	93	58	110	80	85	77	131	119	3	2	39	6	3,540	52	3	158	.	254	72	.	190	45	.	45	102	.	187
30	DURGASHI	942948D	28	157	81	.	118	80	.	.	92	.	.	.	.	.	.	.	.	.	.	167	214	206	144	170	169	38	39	34	107	161	153
31	FARJANA	752635D	26	154	63	.	.	.	120	70	80	87	147	108	1	1	39	3	3,320	49	3	189	.	.	201	.	.	35	.	.	108	.	.
32	FARIYA AMEEN	665162C	27	163	61	7	112	68	120	80	85	.	.	.	1	2	38	3	3,420	49	3	178	.	215	88	.	139	63	.	64	96	.	140
33	FATHIMA ARJUN	480258F	23	146	51	.	111	72	110	70	96	.	.	.	2	1	35	0	1,760	36	.	142	209	226	53	120	209	50	53	47	75	146	148
34	FOUZIA SULTANA	037871D	27	145	70	.	120	74	.	.	92	.	.	.	.	.	.	.	.	.	.	200	220	.	139	175	.	50	52	.	116	151	.
35	GEETHA LASKHMI	482895f	30	151	53	6	94	64	120	70	86	73	108	103	1	2	39	1	2,800	48	.	232	234	295	134	247	357	45	42	46	168	171	184
36	GUNA	395568F	27	150	57	14	99	61	110	80	89	88	158	118	1	1	39	5	3,660	52	3	133	160	187	79	137	171	35	40	39	75	104	132
37	HAJEERA	051311F	21	163	58	16	115	65	120	70	81	.	.	.	1	2	38	.	2,910	48	3	166	258	345	70	158	221	56	69	83	96	182	255
38	HAJIMA	675587C	34	151	53	9	120	80	120	70	83	85	136	111	1	2	40	2	3,320	51	3	181	255	260	92	147	171	59	54	51	124	191	205
39	HAMSA PRIYA	430765F	27	156	41	.	93	60	.	.	71	.	.	.	.	.	.	.	.	.	.	128	.	193	68	.	115	57	.	68	56	.	110
40	HEMALATHA	418283F	25	160	92	13	106	66	120	70	80	71	128	111	3	1	39	4	3,550	51	3	121	159	176	61	118	144	54	76	85	58	69	75
41	INDHUMATHI	254689F	22	152	37	.	82	56	.	.	73	71	97	109	.	.	.	.	.	.	.	213	263	265	122	171	190	52	50	49	124	203	200
42	JAMUNA	155151F	24	167	61	11	99	61	120	70	86	88	173	125	1	1	38	6	2,960	46	.	161	191	196	123	120	197	56	71	73	83	109	90
43	JAYA SHREE	819221C	34	156	73	7	85	58	120	70	77	.	.	.	2	2	37	2	2,820	48	3	106	163	171	52	195	191	40	52	58	54	82	98
44	JOTHILAKSHMI	164686F	28	150	52	10	96	64	110	80	94	80	92	125	2	2	38	6	3,020	49	3	150	240	245	94	215	174	45	54	61	92	171	184
45	KALPANA	418455F	24	160	62	10	125	78	120	80	.	78	126	121	2	1	36	1	1,700	45	2	196	231	236	97	172	230	46	65	83	133	143	120
46	KANCHANA	871182D	22	152	43	13	86	54	100	60	69	67	81	91	1	1	39	1	3,200	49	3	162	233	.	86	164	.	46	57	.	93	156	.
47	KARPAGAM	416153F	24	160	54	18	113	70	110	70	85	80	163	158	2	2	40	3	2,800	49	2	165	201	223	78	204	301	49	58	56	105	135	140
48	KALAISELVI	868076D	34	147	60	15	110	70	120	70	90	78	133	.	3	1	39	.	2,820	48	3	118	185	191	81	147	316	41	65	58	66	110	101
49	KALAIVANI	494065F	20	154	54	14	105	69	110	70	82	76	84	74	3	1	35	5	2,870	49	.	126	173	.	92	159	.	33	45	.	69	110	.

50	KAVITHA N	398894F	25	167	55		96	66			102												113			65			43			62		
51	KOMALA	891186D	27	150	53	10	106	68	120	70	94	86	127	89	1	2	39	1	2,750	48	2	163		196	94		259	63		51	91		122
52	KOMATHI	965404D	28	158	90	3	124	74	120	70		88	132	90	2	1	38	1	3,400	50	3	159	173	213	113	193	264	35	45	47	114	105	138
53	LAKSHMI	478733F	23	169	63		105	62				72	134	105								144	192		71	89		54	67		89	133	
54	LALITHA	393287F	21	155	52	4	110	64	120	70	93	75	131	102	1	2	38	1	2,790	47	3	178		216	109		154	70		72	88		131
55	LATHABAI	021402D	31	156	70	3	103	61	120	80	94				3	1	38	6	3,440	50	3	127	157	138	103	162	156	38	40	40	61	79	69
56	LAVANYA	396744F	25	157	44		94	64			96											135	174	180	43	92	120	50	61	52	71	106	127
57	LAVANYA	392168F	25	155	42	10	98	67	116	70							1	39	2	2,750	47	3	150	179	211	107	198	223	43	46	43	101	109	133
58	LEKHA	473199F	27	153	59		96	62			84											131			79			49			73		
59	MAHALAKSHMI	391489F	20	150	37	14	91	62	120	80	76				1	2	40	2	3,020	48	3	134	194	199	64	151	173	45	48	52	78	137	137
60	MAHALAKSHMI	200472F	27	159	53	13	100	74	120	80	88	77	123	107	1	1	38	2	2,640	47	3	142	142	141	73	114	166	39	48	47	79	79	75
61	MALA	022035C	35	158	66	9	118	82	120	70	87	89	207	176	1	1	40	1	3,430	50	3	164	178	162	156	172	225	38	51	49	97	97	93
62	MAMTHA	277612F	24	148	41	13	105	70	110	80	72	82	118	112	2	1	39	4	3,340	50	3	163	144	155	103	195	242	57	49	45	85	78	85
63	MANJULA	366421D	30	144	38	4	117	84	110	70	92	79	163	118	3	1	37	4	3,020	49	3	147	193	286	59	162	251	57	50	62	84	127	207
64	MANJULA SREENIVAS	391529F	25	150	51	5	117	72	130	80	97				3	1	34	2	1,970	42	3	150	192	155	81	148	125	48	49	41	90	135	102
65	MARY LAVANYA	450065D	27	150	58		96	69				86	174	119								179	169	177	164	244	223	60	54	64	103	91	94
66	MENAKA	455437D	30	162	59		89	56				88										170			162			41			110		
67	MOHANALAKSHMI	413682F	18	159	33	12	105	61	90	60	78				1	2	39	3	2,880	49	2	108	217	256	57	116	196	39	73	74	61	145	169
68	MURUGESWARI	491884D	22	146	60		97	60			70	88	136	101								133	168		125	222		34	46		67	84	
69	MUTHURANI	395263F	20	151	41		100	67			93											150			64			58			74		
70	NALINI	868420D	23	145	60		115	79			81											177	179	204	132	178	219	46	54	50	101	115	115
71	NALINI M	419058F	29	158	53	12	111	78	130	90	88	90	141	133	1	2	38	5	2,770	45	3		246	234		167	172		60	63		172	166
72	NANTHINI	410546F	22	155	41	5	97	62	120	70	93	80	140	94	1	1	38	2	3,140	49	3	140	225	238	84	175	207	47	46	41	79	154	168
73	NAZNEENSULTANA	721646D	27	149	58	8	97	60	120	90	83	80	138	157	3	2	39		3,140	49	3	180	205	221	85	131	139	57	60	72	100	130	138
74	NASEEMA SULTANA	372368F	27	155	48	12	113	74	120	70	91				1	1	39	2	3,110	50	2	110	167		57	163		62	43		41	105	

75	NIRMALA	425680F	33	155	43	-2	89	63	120	70	83	76	163	132	1	2	37	6	3,180	48	3	137	166	224	70	87	197	48	51	50	79	109	159
76	NITHYA	473191F	21	155	62	.	110	67	.	.	89	.	.	.	.	.	.	.	.	.	.	166	190	175	119	175	167	55	54	57	104	112	106
77	NITHYA LAKSHMI	382711F	26	165	62	16	94	62	100	70	91	.	.	.	1	1	40	.	3,100	49	3	183	270	300	53	165	210	57	60	61	109	199	230
78	POOVARASI	410067F	25	150	42	8	116	82	.	.	89	76	188	171	2	1	33	6	1,880	43	2	173	222	.	91	221	.	54	32	.	110	170	.
79	PRABAVATHI	470856F	29	154	54	.	105	69	.	.	.	82	194	181	.	.	.	.	.	.	.	157	213	.	51	125	.	45	62	.	105	139	.
80	PRABAVATHI	478927F	24	165	63	.	105	72	.	.	97	.	.	.	.	.	.	.	.	.	.	152	.	.	121	.	.	37	.	.	96	.	.
81	PRIYA	418934F	26	149	73	12	112	76	120	70	71	79	165	136	2	2	39	1	3,020	48	3	168	193	188	142	177	172	34	44	46	97	142	131
82	PRIYADHARSHANI	869819D	25	157	57	18	86	57	120	70	87	93	141	109	1	2	38	5	4,060	52	3	144	192	.	74	93	.	55	73	.	71	120	.
83	PRIYANKA KUMARI	408991F	25	149	53	12	110	66	.	.	89	83	189	166	1	2	34	3	2,190	46	2	248	383	317	335	620	558	49	55	36	144	272	208
84	RAJAKUMARI	388524F	25	165	60	6	108	67	120	70	81	82	137	120	1	1	39	5	2,780	48	3	193	216	220	82	137	197	68	73	73	112	110	123
85	RAJALAKSHMI	409363F	29	159	69	.	120	80	110	60	97	78	140	132	1	1	36	.	3,230	48	3	191	.	283	102	.	269	64	.	69	112	.	199
86	RAMADEVI	009481D	32	160	50	4	110	70	110	70	88	83	175	193	1	2	36	6	2,420	46	2	172	211	250	85	196	196	58	51	53	97	144	151
87	REKHA	398062F	24	151	52	11	105	68	110	70	94	89	151	149	3	2	39	3	3,280	50	3	174	230	231	110	223	245	57	59	58	102	160	148
88	REVATHI	392153F	26	157	59	6	126	76	130	90	95	88	141	106	2	2	39	2	2,940	48	3	192	262	266	147	222	271	53	52	56	124	182	198
89	REVATHY	529854D	23	158	62	-3	106	61	110	70	80	77	103	92	1	1	40	3	2,790	49	2	148	197	203	86	157	149	43	40	47	88	148	148
90	SANGEETHA	464614D	26	154	70	2	.	.	120	70	80	89	140	101	1	2	39	4	3,100	46	3	152	175	193	86	162	167	42	45	49	96	119	132
91	SARASWATHI	645659D	30	165	53	12	103	62	100	70	.	89	177	87	1	2	38	6	3,400	50	3	163	208	.	82	180	.	55	53	.	102	145	.
92	SAMEENA	478393F	19	153	47	5	98	65	120	70	87	90	148	117	1	2	38	5	2,830	46	.	149	206	211	98	186	214	57	70	67	77	110	115
93	SANKARI	634385B	35	155	83	11	102	76	140	80	98	.	.	.	2	2	34	.	3,140	47	3	155	218	249	110	160	271	59	62	53	85	149	140
94	SARITHA	001364D	31	164	64	16	109	74	110	70	83	85	118	121	1	1	39	1	3,950	50	3	147	200	222	86	185	264	46	60	55	85	128	150
95	SANDHIYA	423912F	20	160	49	13	119	72	120	80	87	73	93	90	1	1	37	2	2,400	47	2	154	.	268	89	.	198	37	.	40	103	.	197
96	SANGEETA S	410685F	23	155	64	.	99	62	.	.	86	.	.	.	.	.	.	.	.	.	.	135	.	.	76	.	.	40	.	.	94	.	.
97	SARANYA	391408F	22	152	37	21	90	60	.	.	84	81	146	129	1	2	40	1	3,250	49	3	192	260	.	115	251	.	48	49	.	109	172	.
98	SATHYA	322680D	29	164	74	2	124	75	140	90	90	76	101	106	3	2	39	5	2,900	49	2	178	.	260	101	.	195	55	.	68	104	.	192
99	SATHIYA	414608F	20	154	59	10	106	66	120	80	78	70	118	105	3	1	38	2	3,140	52	2	140	151	194	123	199	289	35	35	37	92	86	127
100	SATHIYA	896932D	19	157	66	2	107	65	130	90	.	79	174	156	1	1	37	5	3,460	49	3	191	234	310	91	155	270	46	44	49	136	176	228
101	SARANYA	385454F	21	164	51	13	117	71	120	80	85	84	113	125	1	1	40	5	3,170	51	2	126	200	215	71	146	199	40	61	62	71	112	132
102	SELVI	719256B	33	165	58	20	85	56	110	70	79	.	.	.	1	1	38	6	3,100	47	3	161	.	241	132	.	211	47	.	70	81	.	131
103	SHALINI	626838D	23	152	50	.	121	74	140	90	.	90	173	159	1	2	38	4	3,000	50	2	150	243	227	60	154	172	54	56	46	84	147	166
104	SHAMA	405680F	18	155	63	11	95	53	120	80	.	93	139	171	1	1	37	6	2,500	47	2	137	.	226	68	.	255	48	.	71	72	.	133

105	SHAHEEN	473625D	28	157	79	11	100	66	110	60	88	83	151	116	1	1	39	.	3,600	50	3	172	192	191	133	184	183	46	53	56	112	121	123
106	SHAHANAZ	386140F	22	154	59	22	101	60	110	80	76	.	.	.	2	1	39	4	3,400	51	3	157	183	171	96	114	159	46	50	44	94	122	114
107	SHAKILA	947992C	32	152	59	-1	107	63	120	70	87	72	109	83	2	2	37	4	2,360	45	3	207	.	.	75	.	.	45	.	.	148	.	.
108	SHOBANA	909841C	25	163	97	.	116	70	.	.	83	87	160	11	.	.	.	.	.	.	.	158	161	.	196	285	.	33	37	.	92	93	.
109	SHOFIYA SHAZEEYA	906593D	23	162	68	11	127	77	110	70	91	79	136	133	1	2	37	3	2,610	41	4	171	219	245	96	146	113	55	66	63	102	145	148
110	SHARMILA DEVI	437742C	29	156	70	.	103	68	120	70	84	85	123	143	1	2	39	5	3,720	50	3	155	153	172	131	241	228	46	50	52	93	81	100
111	SINDHUBIRAVI	392550F	27	162	35	9	87	61	110	70	84	72	142	139	1	1	39	2	2,310	49	2	185	259	246	76	137	156	74	77	65	102	177	156
112	SUBBULAKSHMI	411255F	28	162	47	7	90	60	.	.	93	.	.	.	3	1	39	2	2,750	.	.	208	226	241	143	195	224	55	50	52	138	168	168
113	SUMATHI	526238D	29	158	59	.	109	80	.	.	.	70	107	93	.	.	.	.	.	.	.	180	234	.	104	212	.	49	71	.	110	147	.
114	SUMITHA D	584717D	30	163	79	11	101	72	120	70	77	84	156	141	1	2	39	1	3,450	52	2	175	187	197	86	198	220	55	42	45	105	118	124
115	SUMITHRA	411114F	18	163	49	20	92	65	120	70	.	82	121	125	2	1	40	1	3,460	49	3	137	.	223	66	.	234	49	.	43	87	.	154
116	THAMIL SELVI	933247C	27	162	60	13	112	77	110	70	.	.	.	.	1	1	39	6	3,730	51	3	159	182	227	67	162	239	52	43	39	94	121	150
117	THAMARAI SELVI	395266F	29	151	59	11	113	76	100	70	182	.	.	.	3	2	38	2	3,200	48	3	197	179	173	96	206	299	35	54	53	142	100	89
118	THANGAM	410615F	28	149	51	8	111	76	.	.	.	.	.	.	1	2	40	.	3,420	49	3	148	.	.	96	.	.	47	.	.	81	.	.
119	THILAGA	899918D	32	159	57	4	111	77	110	70	83	80	153	92	3	2	39	2	3,074	49	3	155	203	198	78	145	119	57	61	66	89	131	124
120	THILAGAVATHI	387357F	27	155	41	.	.	.	120	70	83	78	115	76	1	2	38	5	2,370	46	2	165	190	.	103	150	.	66	72	.	84	108	.
121	UMA MAHESWARI	774252D	32	137	54	11	87	56	110	80	75	.	.	.	1	2	40	1	3,630	51	3	179	.	.	160	.	.	43	.	.	121	.	.
122	UMA	536250D	24	157	42	14	108	67	100	70	82	80	117	131	1	1	39	1	3,400	49	3	216	283	.	112	210	.	57	66	.	118	193	.
123	VASANTHA	098832F	23	159	47	.	91	61	.	.	.	60	143	68	.	.	.	.	.	.	.	109	.	.	54	.	.	43	.	.	63	.	.
124	VANI	592188D	20	157	55	9	94	62	120	70	76	75	143	127	1	2	40	2	4,550	53	3	151	157	170	184	202	260	33	47	42	98	94	106
125	VENNILA	175112F	31	160	61	9	96	67	110	70	.	73	144	104	3	2	40	2	3,380	50	3	165	199	211	99	153	160	38	52	54	114	125	136
126	VIDHYA	409207F	27	159	59	8	99	53	110	70	80	76	116	124	1	2	40	.	3,600	50	3	132	157	186	75	120	132	35	41	42	94	100	132
127	VIJAYALAKSHMI	343700D	28	157	60	16	101	67	110	70	79	76	167	97	1	1	40	2	3,580	50	3	188	223	.	129	153	.	47	50	.	124	153	.
128	VIJAYALAKSHMI	262238F	30	159	57	.	114	70	120	70	84	.	.	.	2	1	38	5	3,320	49	3	161	120	166	180	251	283	41	33	39	90	56	76
129	YASMEEN	505351C	31	153	64	1	98	71	110	70	92	108	162	169	1	2	39	1	2,930	49	2	166	231	229	109	182	214	45	48	47	97	164	160
130	ZUBITHA	433096F	22	147	38	.	101	64	.	.	85	.	.	.	.	.	.	.	.	.	.	142	.	.	81	.	.	52	.	.	77	.	.